Electronic Supplementary Information

Copper-Catalyzed One-pot, Three-component Tandem Conjugative Alkynylation/6-*endo* Cyclization Sequence: Access to Pyrano[2,3-*d*]pyrimidines

Nimmakuri Rajesh and Dipak Prajapati*

Medicinal Chemistry Division, CSIR-North-East Institute of Science & Technology, Jorhat 785006, Assam, India

E-mail: dr_dprajapati2003@yahoo.co.uk

Table of Contents

General information

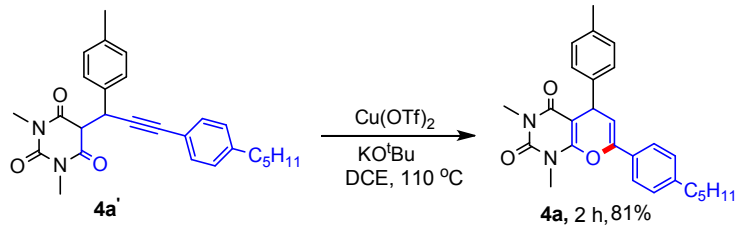
All the commercially available reagents were used as received. IR Spectra were recorded on a SHIMADZU FTIR-8400 instrument. NMR spectra were recorded on Advance DPX 300 MHz FT-NMR spectrometer using tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on ESQUIRE 3000 Mass spectrometer. All the experiments were monitored by thin layer chromatography (TLC). TLC was performed on pre-coated silica gel plates (Merck). After elution, plate was visualized under UV illumination at 254 nm for UV active materials. Further visualization was achieved by staining $KMnO_4$ warming in a hot air oven. Column chromatography was performed on silica gel (100-200 mesh, Merck) using ethyl acetate: hexane as eluent.

Experimental data

General procedure for the synthesis of pyrano[2,3-*d*]pyrimidines *via* tandem conjugative alkynylation/6-*endo* cyclization process *(4a-4w)*:

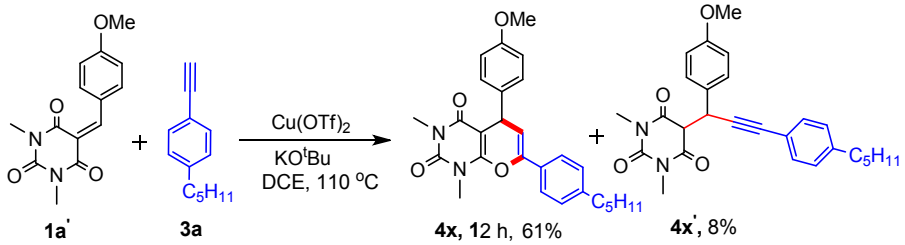
To a mixture of barbituric acid **1** (1 mmol), aldehyde **2** (1 mmol), terminal alkyne **3** (1.2 mmol) in DCE (8ml), add 1.3 equivalents of KO^{t}Bu and 10 mol% $Cu(OTf)_2$. Then, the mixture was stirred at 110 ^oC in DCE till the complete conversion of conjugative addition product takes place. After completion of reaction as indicated by TLC, the crude mixture was cooled down to room temperature and the solvent was distilled off under reduced pressure. The mixture was then quenched with water, and extracted with ethyl acetate (3×15ml). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography by using ethyl acetate and hexane as eluents to furnish the desired products **(4a-4w)**.

Control experiments:



Procedure for cyclization of conjugative addition product 4a':

Conjugative addition product **4a'** (0.5 mmol), KO^{t}Bu (0.6 mmol) and $Cu(OTf)_2$ (5 mol%) were added into a 50 ml round bottomed flask containing DCE (5 ml). Then, the mixture was stirred at 110 °C in DCE for 2 h. After completion of reaction as indicated by TLC, the crude mixture was cooled down to room temperature and the solvent was distilled off under reduced pressure. The mixture was then quenched with water, and extracted with ethyl acetate (3×15ml). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography by using ethyl acetate and hexane as eluents to furnish the desired product **4a** in 81% yield as yellow solid.

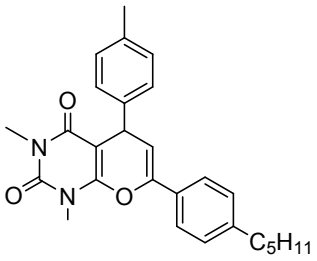


Procedure for synthesis of compound 4x *via* two component reaction strategy:

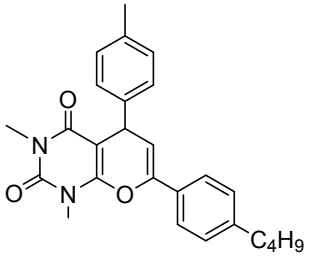
To a mixture of Knoevenagel condensation product *i.e.* barbituric acid derived organic acceptor **1a'** (1 mmol), 1-ethynyl-4-pentyl benzene **3a** (1.2 mmol), in DCE (5ml), add 1.3

equivalents of KO^{t}Bu and 10 mol% $Cu(OTf)_2$. Then, the mixture was stirred at 110 ^oC in DCE till for 12 h. After completion of reaction as indicated by TLC, the crude mixture was cooled down to room temperature and the solvent was distilled off under reduced pressure. The mixture was then quenched with water, and extracted with ethyl acetate (3×15ml). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography by using ethyl acetate and hexane as eluents. Cyclization product **4x** was isolated as yellow solid in 61% yield and conjugative addition product **4x'** in 8% yield.

Characterization data of the Products

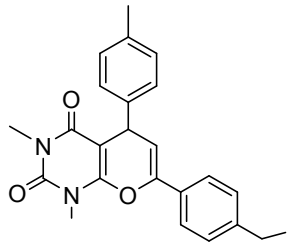


1,3-dimethyl-7-(4-pentylphenyl-5-(*p*-tolyl)prop-2-yne-1-yl)-1H-pyrano[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4a): Yellow solid; m.p. 139.5-140 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 8.2, 1.9 Hz, 2H), 7.24 (ddd, *J* =18.7, 7.1, 4.1 Hz, 4H), 7.12 (d, *J* = 6.9 Hz, 2H), 5.73 (d, *J* = 4.9 Hz, 1H), 4.61 (d, *J* = 4.8 Hz, 1H), 3.59 (s, 3H), 3.28 (s, 3H), 2.63 (t, 2H), 2.30 (s, 3H), 1.72 (m, 2H), 1.32 (m, 4H), 0.89 (t, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.9, 152.6, 150.7, 146.5, 144.4, 141, 136.6, 129.2, 129.1, 128.6, 127.9, 124.2, 103.8, 89.7, 35.9, 35.5, 31.3, 30.9, 28.9, 27.9, 22.4, 21.0, 13.9; MS (GCMS, m/z) 430 $[M]^+$; Anal. Calcd. for $C_{27}H_{30}N_2O_3$: C, 75.32; H, 7.02; N, 6.51. Found: C, 73.34; H, 6.99; N, 6.52.

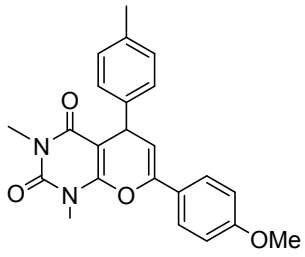


7-(4-butylphenyl)-1,3-dimethyl-5-(*p*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4b): Yellow solid; m.p. 140.5-141.2 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* =

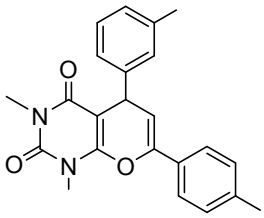
7.3 Hz, 2H), 7.26 (dd, *J* = 4.1, 3.2 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 5.73 (dd, *J* = 4.9, 1.2 Hz, 1H), 4.61 (d, *J* = 4.7 Hz, 1H), 3.60 (s, 3H), 3.28 (s, 3H), 2.64 (t, 2H), 2.31 (s, 3H), 1.66 (m, 2H), 1.36 (dd, *J* = 14.5, 7.2 Hz, 2H), 0.96 (t, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) 161.9, 152.6, 150.7, 146.5, 144.4, 141, 136.6, 129.2, 129.1, 128.6, 127.9, 124.2, 103.8, 89.7, 35.9, 35.2, 33.3, 28.9, 27.9, 22.1, 21, 13.8; MS (GCMS, m/z) 416 $[M]^+$; Anal. Calcd. for $C_{26}H_{28}N_2O_3$: C, 74.97; H, 6.78; N, 6.73. Found: C, 74.95; H, 6.79; N, 6.73.



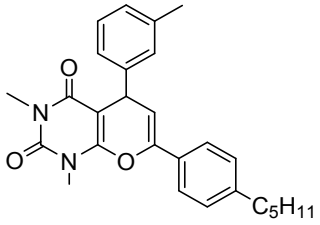
7-(4-ethylphenyl)-1,3-dimethyl-5-(*p*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4c): Yellow solid; m.p. 174-175.5 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.3 Hz, 2H), 7.25 (dd, *J* = 10.3, 6.5 Hz, 4H), 7.12 (d, *J* = 7.9 Hz, 2H), 5.73 (d, *J* = 4.9 Hz, 1H), 4.61 (d, *J* = 4.9 Hz, 1H), 3.59 (s, 3H), 3.28 (s, 3H), 2.68 (q, 2H), 2.30 (s, 3H), 1.25 (t, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.9, 152.6, 150.7, 146.5, 145.7, 141, 136.6, 129.3, 129.1, 128.1, 127.9, 124.3, 103.9, 89.7, 77.2, 76.9, 76.7, 35.9, 28.9, 28.5, 27.9, 21, 15.3; MS (GCMS, m/z) 388 $[M]^+$; Anal. Calcd. for $C_{24}H_{24}N_2O_3$: C, 74.21; H, 6.23; N, 7.21. Found: C, 74.22; H, 6.21; N, 7.21.



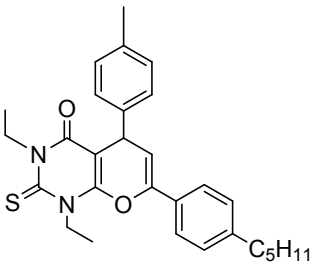
7-(4-methoxyphenyl)-1,3-dimethyl-5-(*p*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4d): Yellow solid; m.p. 138-139.2 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.8 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 7.9 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 5.56 (d, *J* = 4.9 Hz, 1H), 4.52 (d, *J* = 4.9 Hz, 1H), 3.76 (s, 3H), 3.51 (s, 3H), 3.20 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.9, 160.3, 152.6, 150.7, 146.2, 141.1, 136.5, 129.1, 127.9, 125.7, 124.4, 113.9, 102.9, 89.7, 55.2, 35.9, 28.9, 27.9, 21; MS (GCMS, m/z) 390 $[M]^+$; Anal. Calcd. for $C_{23}H_{22}N_2O_4$: C, 70.75; H, 5.68; N, 7.17. Found: C, 70.73; H, 5.68; N, 7.16.



1,3-dimethyl-5-(*m*-tolyl)-7-(*p*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4e): Yellow solid; m.p. 224.4-225 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.20 (ddd, *J* = 28.1, 16.2, 4.7 Hz, 4H), 7.04 (d, *J* = 7.2 Hz, 2H), 5.73 (d, *J* = 4.8 Hz, 1H), 4.60 (d, *J* = 4.8 Hz, 1H), 3.61 (s, 3H), 3.29 (s, 3H), 2.38 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.9, 152.8, 150.7, 146.4, 143.8, 139.3, 138, 129.2, 128.6, 128.3, 127.8, 125.1, 124.2, 103.9, 89.5, 36.3, 28.9, 28, 21.4, 21.2; MS (GCMS, m/z) 374 $[M]^+$; Anal. Calcd. for $C_{23}H_{22}N_2O_3$: C, 73.78; H, 5.92; N, 7.48. Found: C, 73.79; H, 5.90; N, 7.48.

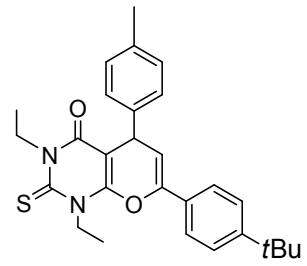


1,3-dimethyl-7-(4-pentylphenyl-5-(*m*-tolyl)prop-2-yne-1-yl)-1*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4f): Yellow solid; m.p. 79-80.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.3 Hz, 2H), 7.28 (m, 5H), 7.03 (d, *J* = 7.0 Hz, 1H), 5.73 (d, *J* = 4.9 Hz, 1H), 4.60 (d, *J* = 4.9 Hz, 1H), 3.60 (s, 3H), 3.29 (s, 3H), 2.68 (m, 2H), 2.32 (s, 3H), 1.69 (m, 2H), 1.40 (m, 4H), 0.89 (t, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.9, 152.8, 150.7, 146.4, 144.4, 143.9, 138, 129.2, 128.6, 128.3, 127.8, 125.1, 124.2, 103.9, 89.5, 36.3, 35.5, 31.3, 30.9, 28.9, 28, 22.4, 21.4, 14; MS (GCMS, m/z) 430 $[M]^+$; Anal. Calcd. for $C_{27}H_{30}N_2O_3$: C, 75.32; H, 7.02; N, 6.51. Found: C, 73.34; H, 7.03; N, 6.49.

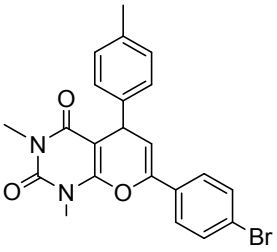


1,3-diethyl-7-(4-pentylphenyl)-2-thioxo-5-(*p*-tolyl)-2,3-dihydro-1*H*-pyrano[2,3-*d*]pyrimidin-4(5*H*)-one (4g): Reddish gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 6.5 Hz, 2H), 7.24 (dd, *J* = 9.8, 3.9 Hz, 4H), 7.13 (d, *J* = 6.9 Hz, 2H), 5.75 (d, *J* = 4.9 Hz, 1H), 4.86 (m, 2H), 4.63 (d, *J* = 4.8 Hz, 1H), 4.56 (m, 1H), 4.43 (m 1H), 2.63 (t, 2H), 2.31 (s, 3H), 1.66 (m, 2H), 1.50 (t, 3H), 1.35 (m, 4H), 1.25 (t, 3H), 0.89 (t, 3H); ^{13}C NMR (126 MHz,

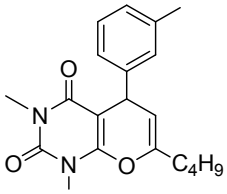
$CDCl_3$) δ 175, 159.8, 152.6, 146.7, 144.5, 140.4, 136.7, 129.2, 129, 128.8, 127.9, 124.1, 103.6, 94.4, 44.6, 43.5, 35.9, 35.5, 31.3, 30.9, 22.4, 21, 13.9, 12.8, 11.4; MS (GCMS, m/z) 474 $[M]^+$; Anal. Calcd. for $C_{29}H_{34}N_2O_2S$: C, 73.38; H, 7.22; N, 5.90. Found: C, 73.39; H, 7.21; N, 5.87.



7-(4-(tert-butyl)phenyl)-1,3-diethyl-2-thioxo-5-(*p*-tolyl)-2,3-dihydro-1*H*-pyrano[2,3-*d*]pyrimidin-4(5*H*)-one (4h): Orangish yellow solid; m.p. 98.1-99 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J*=8.6 Hz, 2H), 7.27 (m, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 5.76 (d, *J* = 4.9 Hz, 1H), 4.81 (dd, *J* = 14.5, 7.1 Hz, 2H), 4.63 (d, *J* = 4.9 Hz, 1H), 4.57 (m, 1H), 4.49 (m, 1H), 2.31 (s, 3H), 1.50 (t, 3H), 1.34 (s, 9H), 1.24 (t, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175, 159.7, 152.7, 152.6, 146.6, 140.4, 136.7, 129.2, 128.8, 128, 125.7, 123.9, 103.6, 94.4, 44.6, 43.5, 35.9, 34.6, 31, 21, 12.8, 11.4; MS (GCMS, m/z) 460 $[M]^+$; Anal. Calcd. for $C_{28}H_{32}N_2O_2S$: C, 73.01; H, 7.00; N, 6.08. Found: C, 73.04; H, 7.02; N, 6.04.

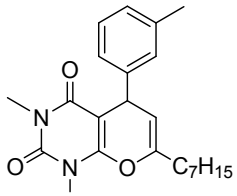


7-(4-bromophenyl)-1,3-dimethyl-5-(*p*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4i): Yellow solid; m.p. 218-219 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H), 7.25 (dd, *J* = 9.4, 4.4 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 5.79 (d, *J* = 4.9 Hz, 1H), 4.61 (d, *J* = 4.9 Hz, 1H), 3.59 (s, 3H), 3.28 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8, 152.5, 150.6, 145.5, 140.6, 136.8, 131.8, 130.7, 129.2, 127.8, 125.8, 123.3, 105.3, 89.5, 36, 29, 28, 21; MS (GCMS, m/z) 440 [M]+; Anal. Calcd. for $C_{22}H_{19}BrN_2O_3$: C, 60.15; H, 4.36; N, 6.38. Found: C, 60.14; H, 4.35; N, 6.41.



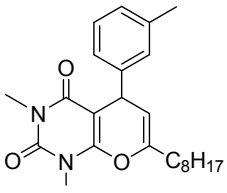
7-butyl-1,3-dimethyl-5-(*m*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4j):

Yellow gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (t, 1H), 7.00 (m, 2H), 6.93 (d, *J* = 7.3 Hz, 1H), 4.92 (d, *J* = 3.9 Hz, 1H), 4.33 (d, *J* = 3.8 Hz, 1H), 3.37 (s, 3H), 3.18 (s, 3H), 2.25 (s, 3H), 2.19 (t, 2H), 1.53 (m, 2H), 1.31 (dd, *J* = 14.7, 7.4 Hz, 2H), 0.86 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 153, 150.8, 148.9, 144.5, 137.9, 128.6, 128.3, 127.6, 125, 104.6, 89.5, 36.1, 32, 28.8, 28., 28, 22, 21.4, 13.7; MS (GCMS, m/z) 340.1 $[M]^+$; Anal. Calcd. for $C_{20}H_{24}N_2O_3$: C, 70.56; H, 7.11; N, 8.23. Found: C, 70.57; H, 7.15; N, 8.26.



7-heptyl-1,3-dimethyl-5-(*m*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4k):

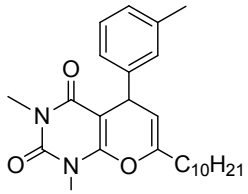
Reddish gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, *J* = 7.5 Hz, 1H), 7.09 (m, 2H), 7.01 (d, *J* = 7.4 Hz, 1H), 5.00 (d, *J* = 4.6 Hz, 1H), 4.41 (d, *J* = 4.5 Hz, 1H), 3.45 (s, 3H), 3.25 (s, 3H), 2.33 (s, 3H), 2.26 (t, 2H), 1.64 (m, 2H), 1.29 (m, 8H), 0.88 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 153, 150.9, 148.9, 144.4, 138, 128.6, 128.3, 127.7, 125, 104.6, 89.5, 77.5, 77, 76.6, 36.1, 32.2, 31.7, 28.9, 28.8, 28, 26.4, 22.6, 21.4, 14; MS (GCMS, m/z) 382 $[M]^+$; Anal. Calcd. for $C_{23}H_{30}N_2O_3$: C, 72.22; H, 7.91; N, 7.32. Found: C, 72.26; H, 7.88; N, 7.35.



1,3-dimethyl-7-octyl-5-(*m*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4l):

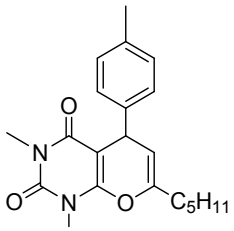
Dark yellow gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (t, 1H), 7.01 (m, 2H), 6.93 (d, *J* = 7.3 Hz, 1H), 4.92 (d, *J* = 4.5 Hz, 1H), 4.33 (d, *J* = 4.3 Hz, 1H), 3.37 (s, 3H), 3.18 (s, 3H), 2.25 (s, 3H), 2.18 (t, 2H), 1.54 (m, 2H), 1.19 (m, 10H), 0.80 (t, 3H).; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 153, 150.8, 148.9, 144.4, 137.9, 128.6, 128.3, 127.7, 125, 104.6, 89.5, 77.5, 77.1, 76.6, 36.1, 32.2, 31.8, 29.3, 29.2, 28.8, 28.8, 28, 26.4, 22.6, 21.4, 14.1; MS (GCMS, m/z) 396.2

[M]$^+$; Anal. Calcd. for $C_{24}H_{32}N_2O_3$: C, 72.70; H, 8.13; N, 7.06. Found: C, 72.66; H, 8.14; N, 7.07.



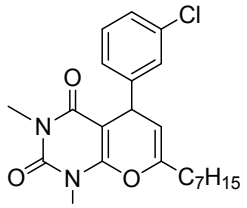
7-decyl-1,3-dimethyl-5-(*m*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4m):

Light reddish gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (t, 1H), 7.09 (m, 2H), 7.01 (d, J = 7.4 Hz, 1H), 5.00 (d, J = 4.5 Hz, 1H), 4.40 (d, J = 4.4 Hz, 1H), 3.45 (s, 3H), 3.25 (s, 3H), 2.33 (s, 3H), 2.26 (t, 2H), 1.60 (m, 2H), 1.28 (m,12H), 0.90 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ162.1, 153, 150.8, 148.9, 144.4, 137.9, 128.6, 128.3, 127.7, 125, 104.6, 89.5, 36.1, 32.2, 31.8, 29.5, 29.5, 29.3, 28.8, 28.8, 28, 26.4, 22.6, 21.4, 14.1; MS (GCMS, m/z) 424.2 [M]$^+$; Anal. Calcd. for $C_{26}H_{36}N_2O_3$: C, 73.55; H, 8.55; N, 6.60. Found: C, 73.58; H, 8.59; N, 6.57.



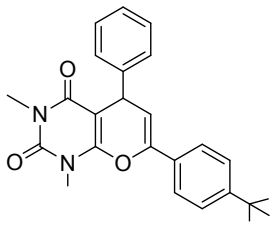
1,3-dimethyl-7-pentyl-5-(*p*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4n):

Yellowish gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (d, J = 7.8 Hz, 2H), 7.11 (d, J =7 .9 Hz, 2H), 5.00 (d, J = 4.5 Hz, 1H), 4.41 (d, J = 4.4 Hz, 1H), 3.44 (s, 3H), 3.25 (s, 3H), 2.30 (s, 3H), 1.63 (m, 2H), 1.33 (m, 6H), 0.90 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 152.9, 150.8, 148.9, 141.6, 136.4, 129.1, 128.7, 128.4, 127.8, 104.5, 89.7, 35.7, 32.2, 31.0, 28.8, 28, 26.1, 22.3, 21, 13.9; MS (GCMS, m/z) 354.2 [M]$^+$; Anal. Calcd. for $C_{21}H_{26}N_2O_3$: C, 71.16; H, 7.39; N, 7.90. Found: C, 71.19; H, 7.37; N, 7.94.

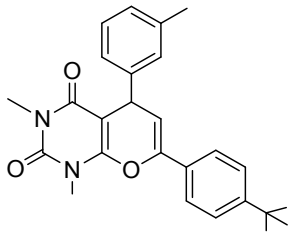


5-(3-chlorophenyl)-7-heptyl-1,3-dimethyl-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4o): Yellow gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (m, 4H), 4.90 (d, J = 4.4 Hz, 1H), 4.36 (d, J = 4.4 Hz, 1H), 3.38 (s, 3H), 3.19 (s, 3H), 2.20 (t, 2H), 1.6 (m, 2H), 1.34 (m, 8H), 0.80 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162, 153.1, 150.7, 149.5, 146.5, 134.3, 129.6, 128, 127, 126.5, 126.3, 103.8, 88.9, 36, 32.2, 31.7, 28.9, 28.8, 28.8, 28, 26.3, 22.5, 14; MS

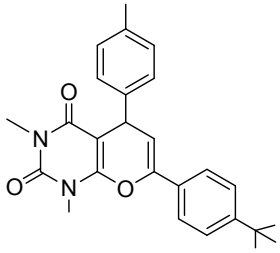
(GCMS, m/z) 402.1 $[M]^+$; Anal. Calcd. for $C_{22}H_{27}ClN_2O_3$: C, 65.58; H, 6.75; N, 6.95. Found: C, 65.56; H, 6.79; Cl, N, 6.91.



7-(4-(*tert*-butylphenyl)-1,3-dimethyl-5-phenyl-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4p): Yellow solid; m.p. 147-148 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.3 (m, 5H), 5.76 (d, *J* = 4.9 Hz, 1H), 4.65 (d, *J* = 4.8 Hz, 1H), 3.6 (s, 3H), 3.28 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162, 152.8, 152.7, 150.8, 146.8, 144, 129.1, 128.5, 128.2, 127, 125.7, 124.2, 103.9, 89.7, 36.5, 34.7, 31.2, 29, 28.1; MS (GCMS, m/z) 402.1 $[M]^+$; Anal. Calcd. for $C_{25}H_{26}N_2O_3$: C, 74.60; H, 6.51; N, 6.96. Found: C, 74.64; H, 6.53; N, 6.93.

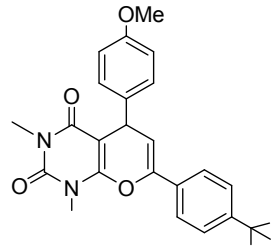


7-(4-(*tert*-butylphenyl)-1,3-dimethyl-5-(*m*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4q): Yellow solid; m.p. 168-169.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.17 (dd, *J* = 10.8, 8.8 Hz, 3H), 7.03 (d, *J* = 6.8 Hz, 1H), 5.74 (d, *J* = 4.9 Hz, 1H), 4.61 (d, *J* = 4.8 Hz, 1H), 3.6 (s, 3H), 3.29 (s, 3H), 2.32 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162, 152.9, 152.7, 150.8, 146.6, 144, 138.1, 129.1, 128.8, 128.4, 127.9, 125.6, 125.3, 124.2, 104.1, 89.7, 36.5, 34.7, 31.2, 29, 28.1, 21.5; MS (GCMS, m/z) 416 $[M]^+$; Anal. Calcd. for $C_{26}H_{28}N_2O_3$: C, 74.97; H, 6.78; N, 6.73. Found: C, 74.98; H, 6.75; N, 6.77.

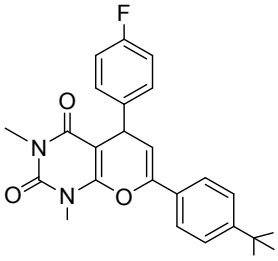


7-(4-(*tert*-butylphenyl)-1,3-dimethyl-5-(*p*-tolyl)-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4r): Colourless gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.36, (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.4 Hz, 2H), 7.04 (d, *J* = 7.6 Hz, 2H), 5.66 (d, *J* = 4.8 Hz, 1H), 4.54 (d, *J* = 4.7 Hz, 1H), 3.52 (s, 3H), 3.21 (s, 3H), 2.23 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (75

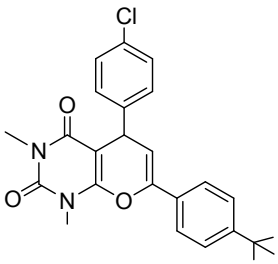
MHz, $CDCl_3$) δ 162, 152.8, 152.7, 150.8, 146.6, 141.1, 136.7, 129.2, 129.1, 128, 125.6, 124.2, 104.1, 89.8, 36, 34.7, 31.2, 29, 28, 21; MS (GCMS, m/z) 416.2 $[M]^+$; Anal. Calcd. for $C_{26}H_{28}N_2O_3$: C, 74.97; H, 6.78; N, 6.73. Found: C, 74.99; H, 6.74; N, 6.79.



7-(4-(*tert*-butylphenyl)-5-(4-methoxyphenyl)-1,3-dimethyl-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4s): Yellow gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 5.74 (d, *J* = 4.9 Hz, 1H), 4.6 (d, *J* = 4.84 Hz, 1H), 3.86 (s, 3H), 3.75 (s, 3H), 3.58 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 158.6, 152.7, 150.8, 146.6, 136.2, 129.26, 129.20, 125.7, 124.2, 113.9, 104.1, 89.9, 55.2, 35.6, 34.7, 31.2, 29, 28; MS (GCMS, m/z) 432.2 $[M]^+$; Anal. Calcd. for $C_{26}H_{28}N_2O_4$: C, 72.20; H, 6.53; N, 6.48. Found: C, 72.17; H, 6.55; N, 6.51.

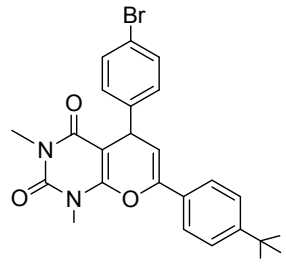


7-(4-(*tert*-butylphenyl)-5-(4-fluorophenyl)-1,3-dimethyl-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4t): Light yellowish gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.24 (dd, *J* = 8.3, 5.4 Hz, 2H), 6.89 (t, 2H), 5.64 (d, *J* = 4.8 Hz, 1H), 4.55 (d, *J* = 4.8 Hz, 1H), 3.5 (s, 3H), 3.1 (s, 3H), 1.25 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 160.2, 152.9, 152.8, 150.7, 146.9, 139.8, 139.7, 129.8, 129.7, 128.9, 125.7, 124.3, 115.4, 115.1, 103.7, 89.6, 35.8, 34.7, 31.1, 29, 28.1; MS (GCMS, m/z) 420 $[M]^+$; Anal. Calcd. for $C_{25}H_{25}FN_2O_3$: C, 71.41; H, 5.99; N, 6.66. Found: C, 71.45; H, 6.03; N, 6.64.

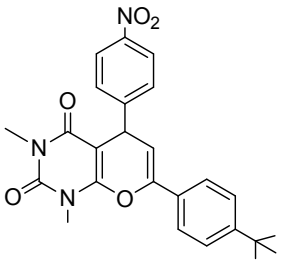


7-(4-(*tert*-butylphenyl)-5-(4-chlorophenyl)-1,3-dimethyl-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4u): Yellow solid; m.p. 148-150 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 5 Hz, 4H), 5.71 (d, *J* = 4.7 Hz, 1H), 4.63 (d, *J* = 4.6 Hz, 1H), 3.59 (s, 3H), 3.28 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$)

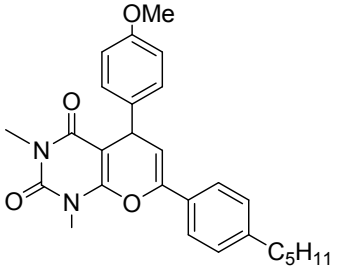
δ 162, 152.9, 152.9, 150.7, 147, 142.5, 132.8, 129.5, 128.9, 128.6, 125.7, 124.3, 103.4, 89.3, 36, 34.8, 31.2, 29, 28.1; MS (GCMS, m/z) 436.1[M]$^+$; Anal. Calcd. for $C_{25}H_{25}ClN_2O_3$: C, 68.72; H, 5.77; N, 6.41. Found: C, 68.75; H, 5.79; N, 6.38.



5-(4-bromophenyl)-7-(4-(*tert*-butylphenyl)-1,3-dimethyl-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4v): Yellow solid; m.p. 155-157 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.4 Hz, 2H), 7.48 (m, 4H), 7.25 (d, *J* = 8.1 Hz, 2H), 5.7 (d, *J* = 4.8 Hz, 1H), 4.62 (d, *J* = 4.8 Hz, 1H), 3.59 (s, 3H), 3.29 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 153, 152.9, 150.7, 147.1, 143, 131.6, 129.9, 128.9, 125.7, 124.3, 120.9, 103.3, 89.2, 36.1, 34.7, 31.1, 29, 28.1; MS (GCMS, m/z) 480 [M]$^+$; Anal. Calcd. for $C_{25}H_{25}BrN_2O_3$: C, 62.38; H, 5.23; N, 5.82. Found: C, 62.39; H, 5.27; N, 5.79.

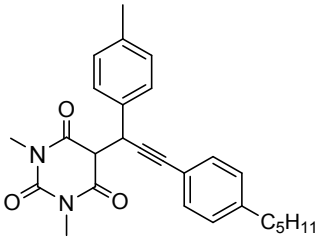


7-(4-(*tert*-butylphenyl)-1,3-dimethyl-5-(4-nitrophenyl)-1*H*-pyrano[2,3-*d*]pyrimidin-2,4(3*H*,5*H*)-dione (4w): Yellow solid; m.p. 173-174.5 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.4 Hz, 2H), 7.53 (dd, *J* = 8.6, 3.3 Hz, 4H), 7.46 (d, *J* = 8.3 Hz, 2H), 5.7 (d, *J* = 4.6 Hz, 1H), 4.78 (d, *J* = 4.6 Hz, 1H), 3.62 (s, 3H), 3.28 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 153.3, 153.2, 151.2, 150.6, 147.7, 146.9, 129.1, 128.6, 125.8, 124.3, 123.8, 102.2, 88.5, 77.4, 77, 76.6, 36.6, 34.8, 31.1, 29.1, 28.1; MS (GCMS, m/z) 447.1 [M]$^+$; Anal. Calcd. for $C_{25}H_{25}N_3O_5$: C, 67.10; H, 5.63; N, 9.39. Found: C, 67.08; H, 5.65; N, 9.42.

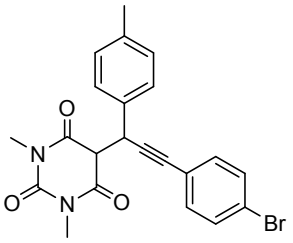


5-(4-methoxyphenyl)-1,3-dimethyl-7-(4-pentylphenyl)-1*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*,5*H*)-dione (4x): Yellow solid; m.p. 126-127 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42

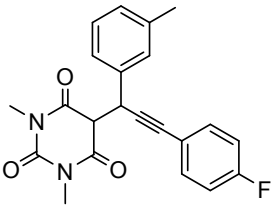
(d, *J* = 7.9 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.77 (d, *J* = 8.3 Hz, 2H), 5.65 (d, *J* = 4.9 Hz, 1H), 4.52 (d, *J* = 4.9 Hz, 1H), 3.69 (s, 3H), 3.52 (s, 3H), 3.21 (s, 3H), 2.61 (m, 2H), 1.55 (m, 2H), 1.25 (m, 4H), 0.82 (t, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.9, 158.4, 152.5, 150.7, 146.5, 144.4, 136.1, 129.2, 129.1, 128.6, 124.2, 113.7, 103.8, 89.8, 55.1, 35.5, 35.5, 31.3, 30.9, 28.9, 27.9, 22.4, 13.9; MS (GCMS, m/z) 446.2 $[M]^+$; Anal. Calcd. for $C_{27}H_{30}N_2O_4$: C, 72.62; H, 6.77; N, 6.27. Found: C, 72.62; H, 6.76; N, 6.29.



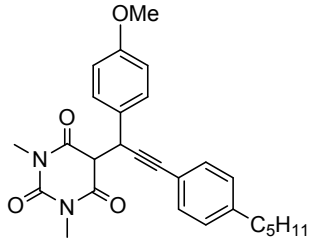
5-(1-(4-butylphenyl)-1-(*p*-tolyl)prop-2-yn-1-yl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,6*H*)-trione (4a'): Reddish gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 4.73 (d, *J* = 3.7 Hz, 1H), 3.79 (d, *J* = 3.7 Hz, 1H), 3.20 (s, 3H), 3.16 (s, 3H), 2.54 (t, 2H), 2.27 (s, 3H), 1.57 (m, 2H), 1.23 (m, 4H), 0.81 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167, 166.1, 151.5, 143.7, 137.9, 132.9, 131.4, 130.1, 129.2, 129.1, 129, 128.4, 127.6, 127, 119.1, 87.3, 83.7, 55.9, 42.4, 35.7, 31.3, 30.8, 28.4, 28.2, 22.4, 21, 13.9; MS (GCMS, m/z) 430 [M]+; Anal. Calcd. for $C_{27}H_{30}N_2O_3$: C, 75.32; H, 7.02; N, 6.51. Found: C, 75.34; H, 7.06; N, 6.50.



5-(3-(4-bromophenyl)-1-(*p*-tolyl)prop-2-yn-1-yl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4i'): Yellow gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.23 (m, 2H), 7.15 (d, *J* = 6.9 Hz, 2H), 7.09 (d, *J* = 7.9 Hz, 2H), 4.72 (d, *J* = 3.5 Hz, 1H), 3.81 (d, *J* = 3.7 Hz, 1H), 3.17 (s, 3H), 3.14 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (126 MHz, CDCl3) δ 166.5, 166.1, 151.3, 138.2, 133, 132.3, 131.5, 129.2, 127.5, 122.8, 121, 86.1, 85.7, 55.6, 42.1, 28.3, 28.2, 21; MS (GCMS, m/z) 440 [M]+; Anal. Calcd. for $C_{22}H_{19}BrN_2O_3$: C, 60.15; H, 4.36; N, 6.38. Found: C, 60.19; H, 4.35; N, 6.43.

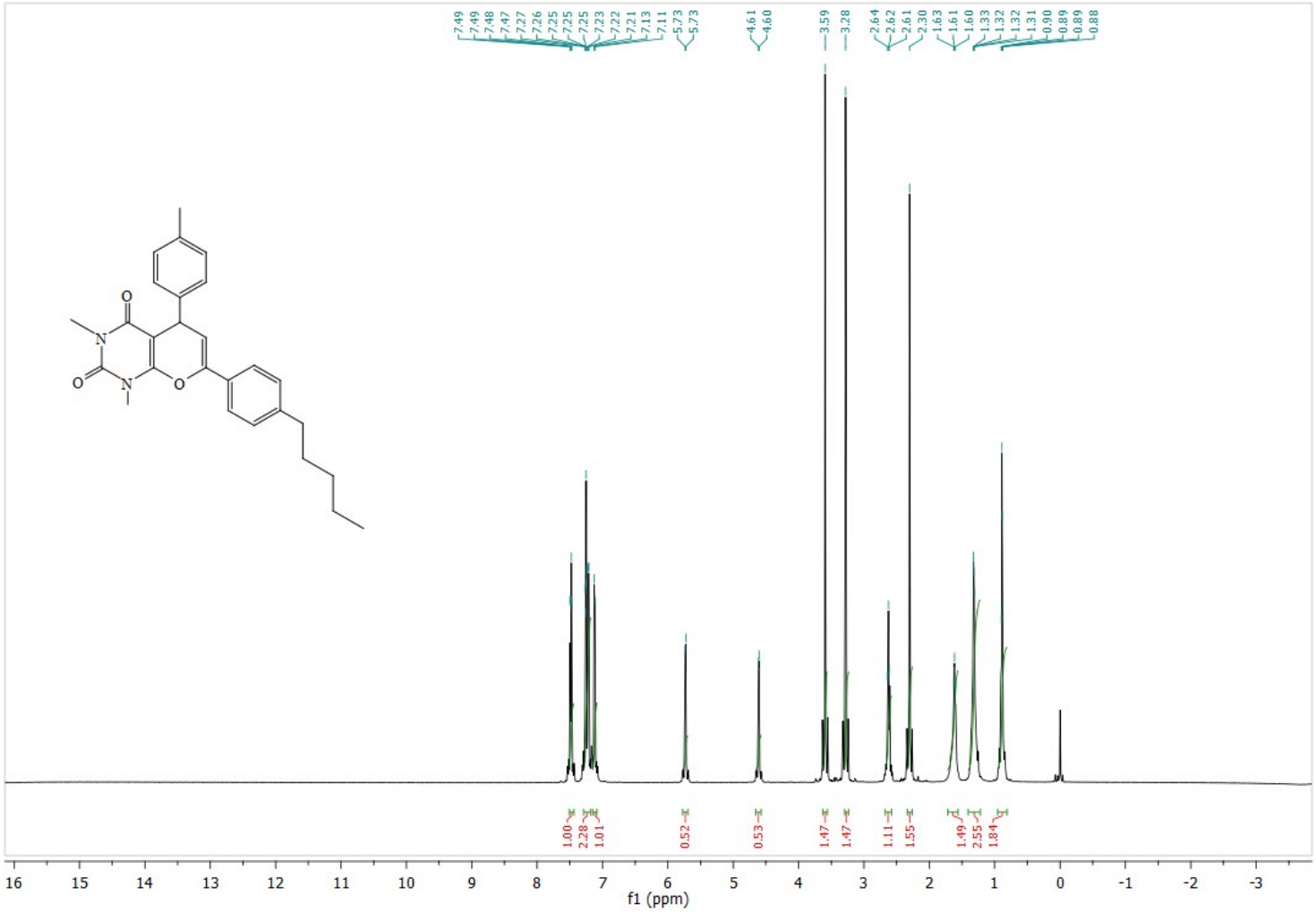


5-(3-(4-fluorophenyl)-1-(*m*-tolyl)prop-2-yn-1-yl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4ii'): Yellow gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (m, 2H), 7.21 (m, 1H), 7.07 (m, 3H), 6.94 (t, 2H), 4.70 (d, *J* = 2.8 Hz, 1H), 3.82 (d, *J* = 3.2 Hz, 1H), 3.15 (s, 3H), 3.13 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 166.3, 164.3, 151.4, 138.4, 135.5, 133.7, 133.6, 129.2, 128.5, 128.4, 124.8, 118.4, 115.8, 115.5, 85.9, 84.6, 55.8, 42.5, 29.6, 28.4, 28.2, 21.4; MS (GCMS, m/z) 378.1 $[M]^+$; Anal. Calcd. for $C_{22}H_{19}FN_2O_3$: C, 69.83; H, 5.06; N, 7.40. Found: C, 69.89; H, 5.01; N, 7.37.

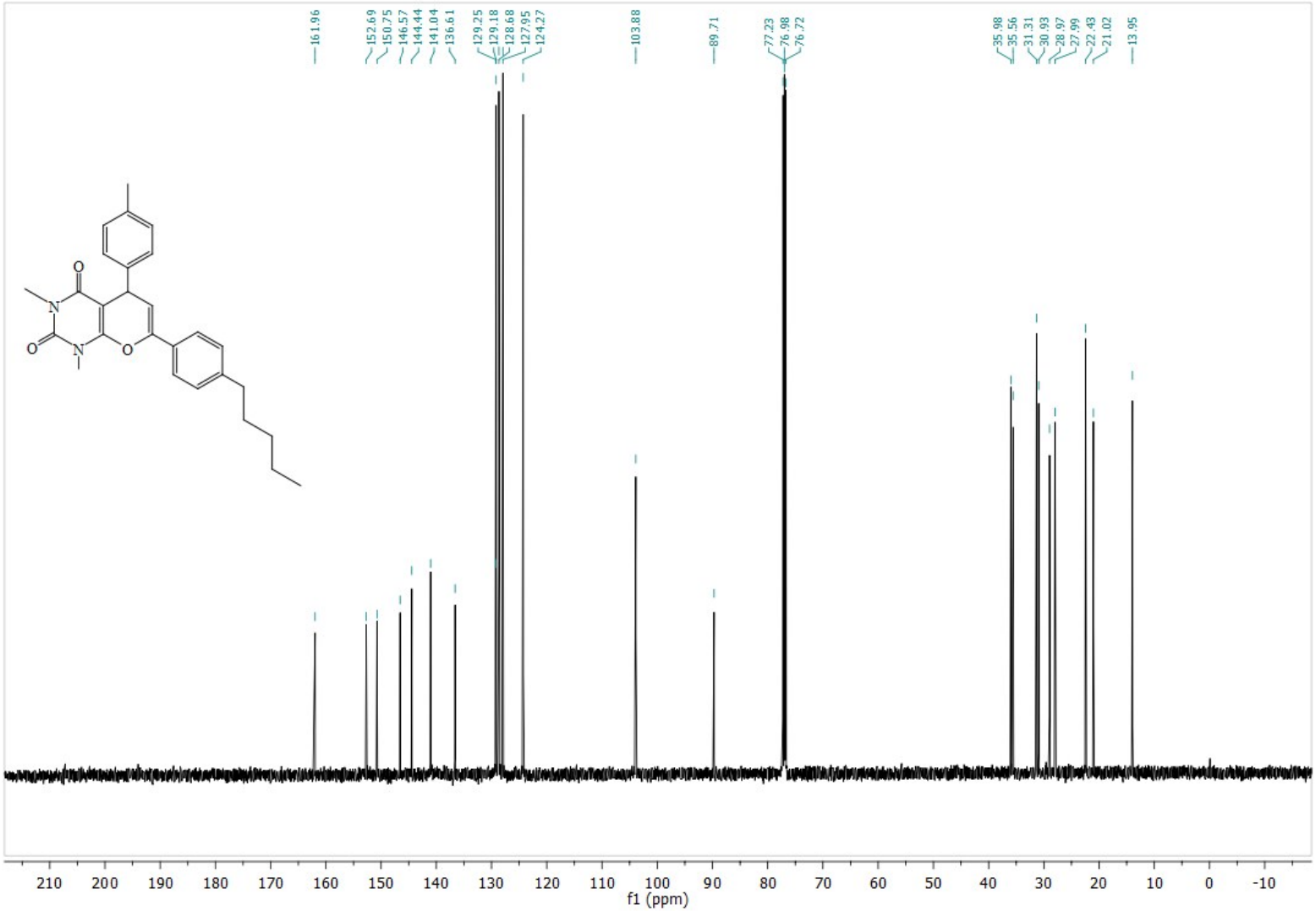


5-(1-(4-methoxyphenyl)-3-(4-pentylphenyl)prop-2-yn-1-yl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (4x'): Yellow gum; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 6.8, 5.0 Hz, 4H), 7.06 (d, *J* = 7.0 Hz, 2H), 6.81 (d, *J* = 7.0 Hz, 2H), 4.73 (d, *J* = 3.2 Hz, 1H), 3.78 (d, *J* = 2.0 Hz, 1H), 3.74 (s, 3H), 3.21 (s, 3H), 3.17 (s, 3H), 2.57 (m, 2H), 1.57 (m, 2H), 1.22 (m, 4H), 0.82 (t, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 166.1, 159.3, 151.5, 143.7, 131.4, 128.9, 128.4, 127.8, 119.1, 113.8, 87.2, 83.8, 56, 55.1, 42, 35.7, 31.2, 30.8, 29.5, 28.3, 28.2, 22.4, 13.9.MS (GCMS, m/z) 446.2 $[M]^+$; Anal. Calcd. for $C_{27}H_{30}N_2O_4$: C, 72.62; H, 6.77; N, 6.27. Found: C, 72.62; H, 6.76; N, 6.29.

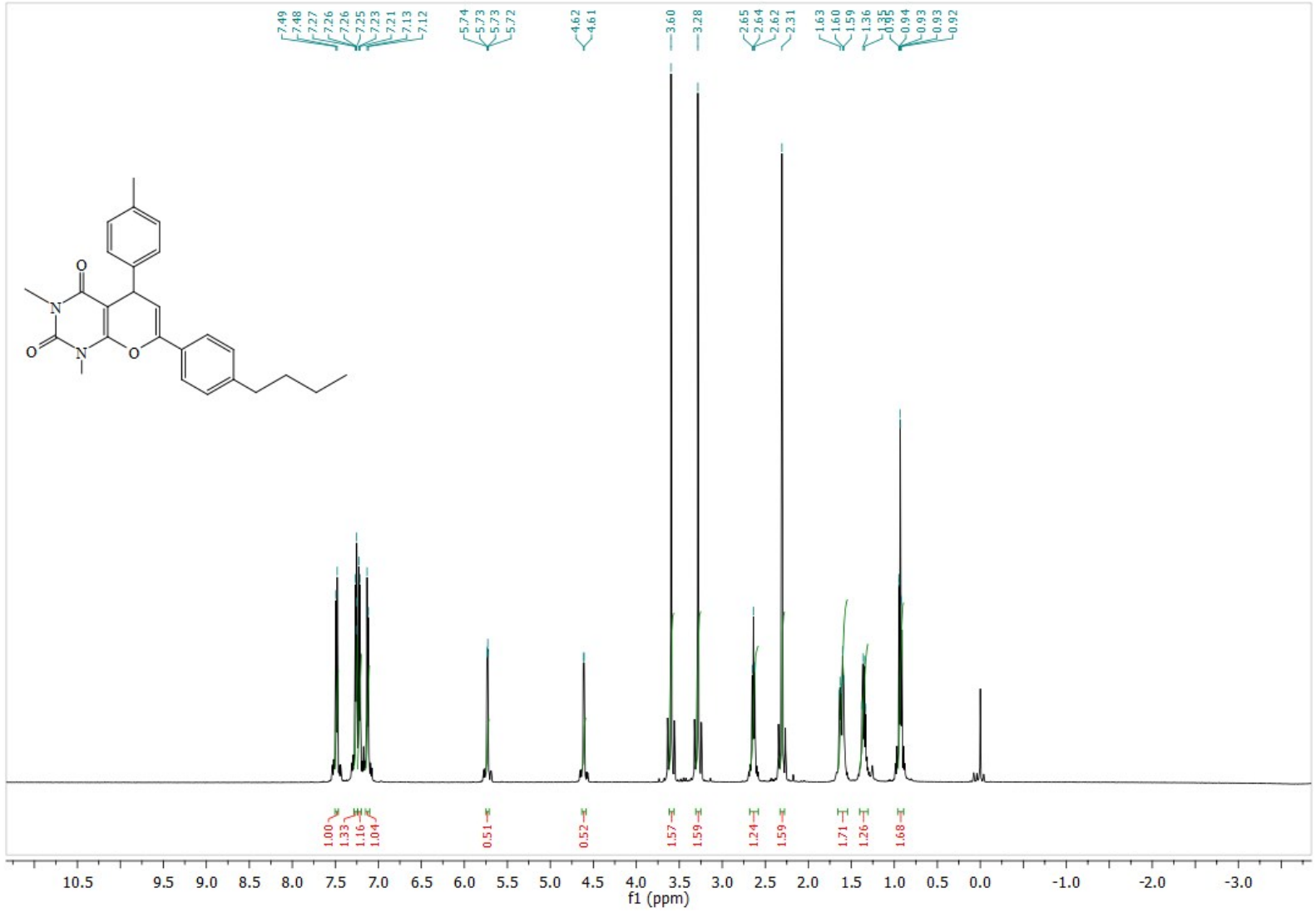
Spectral copies



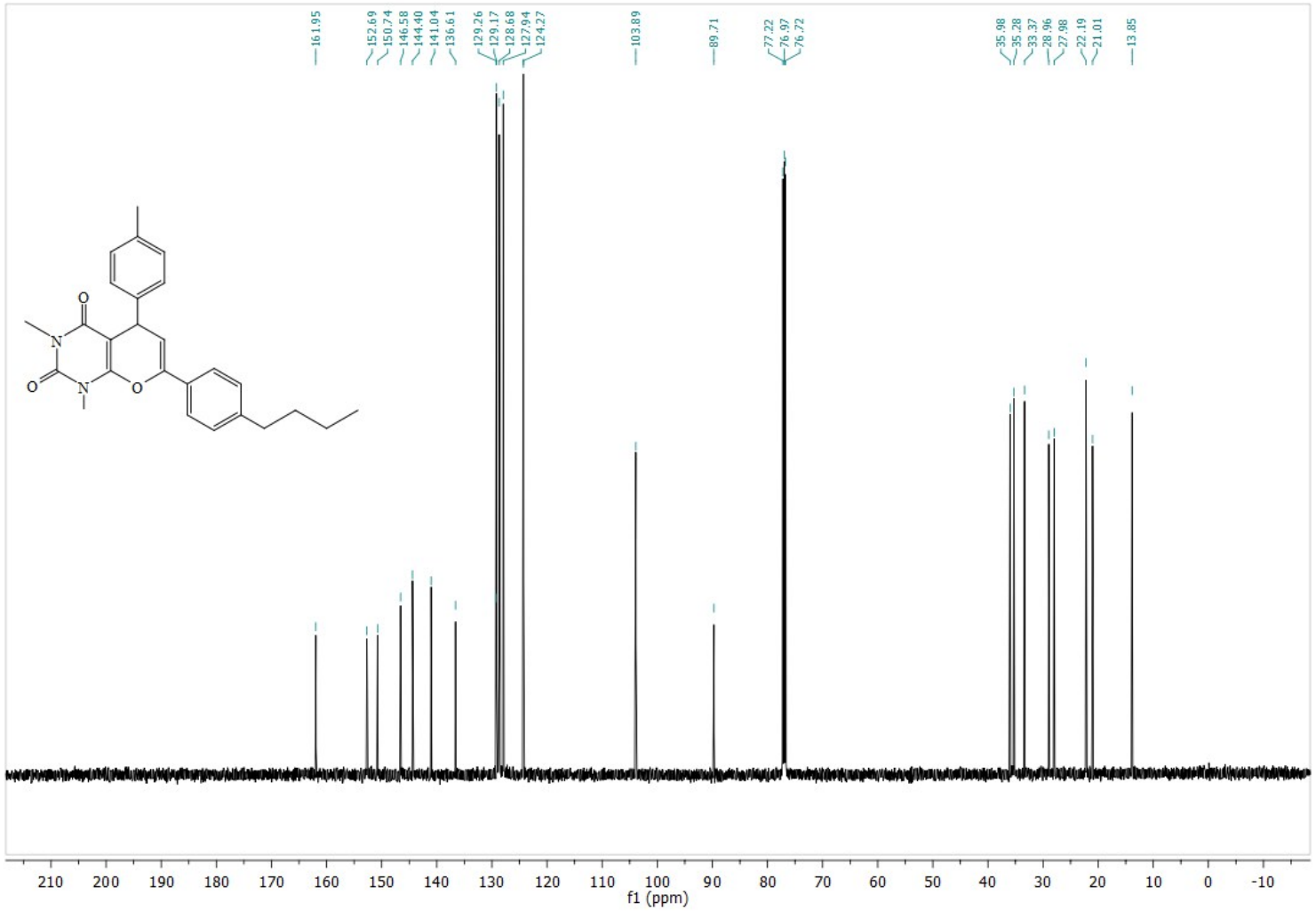
^{1}H NMR Spectrum of compound 4a



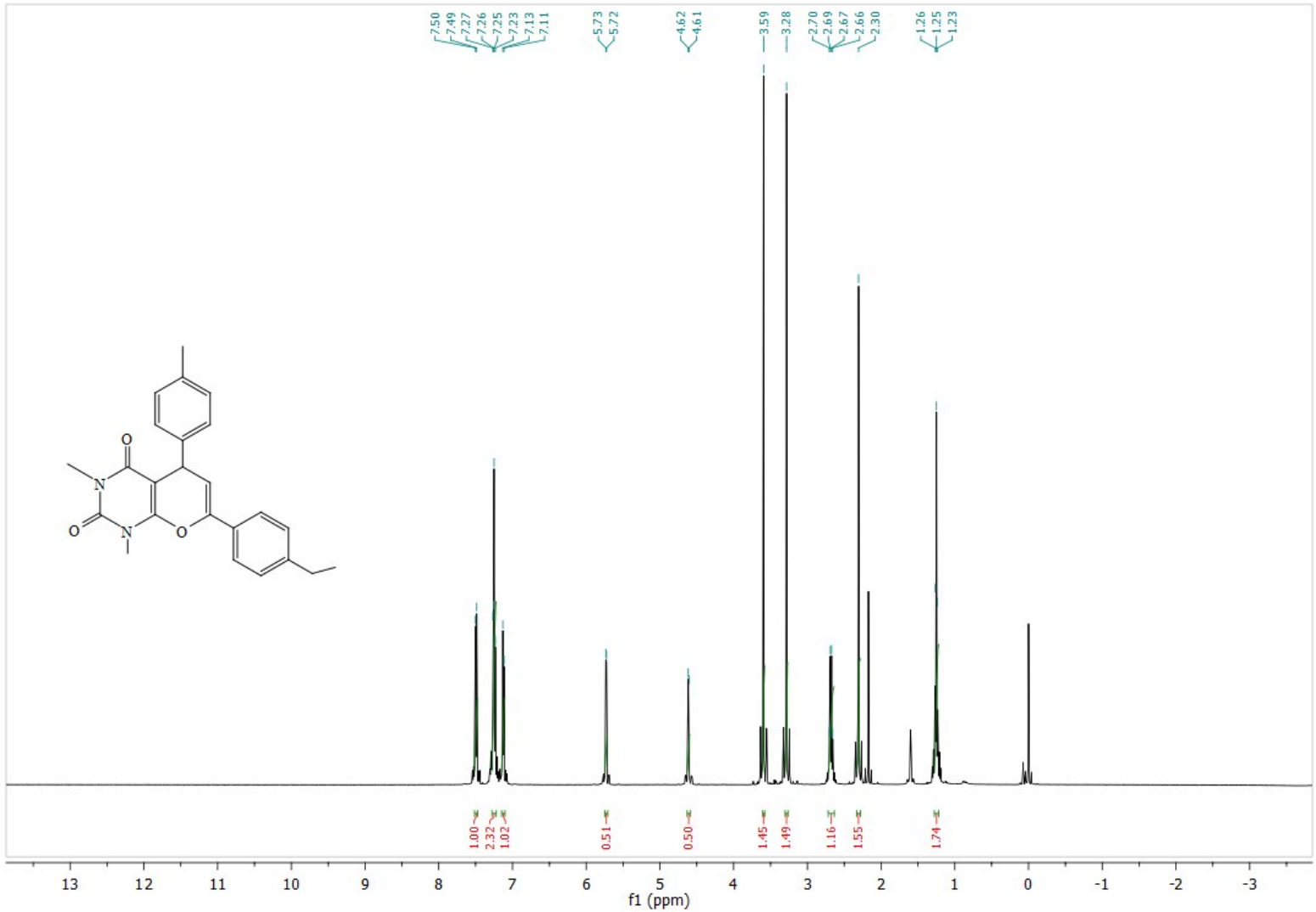
^{13}C NMR Spectrum of compound 4a



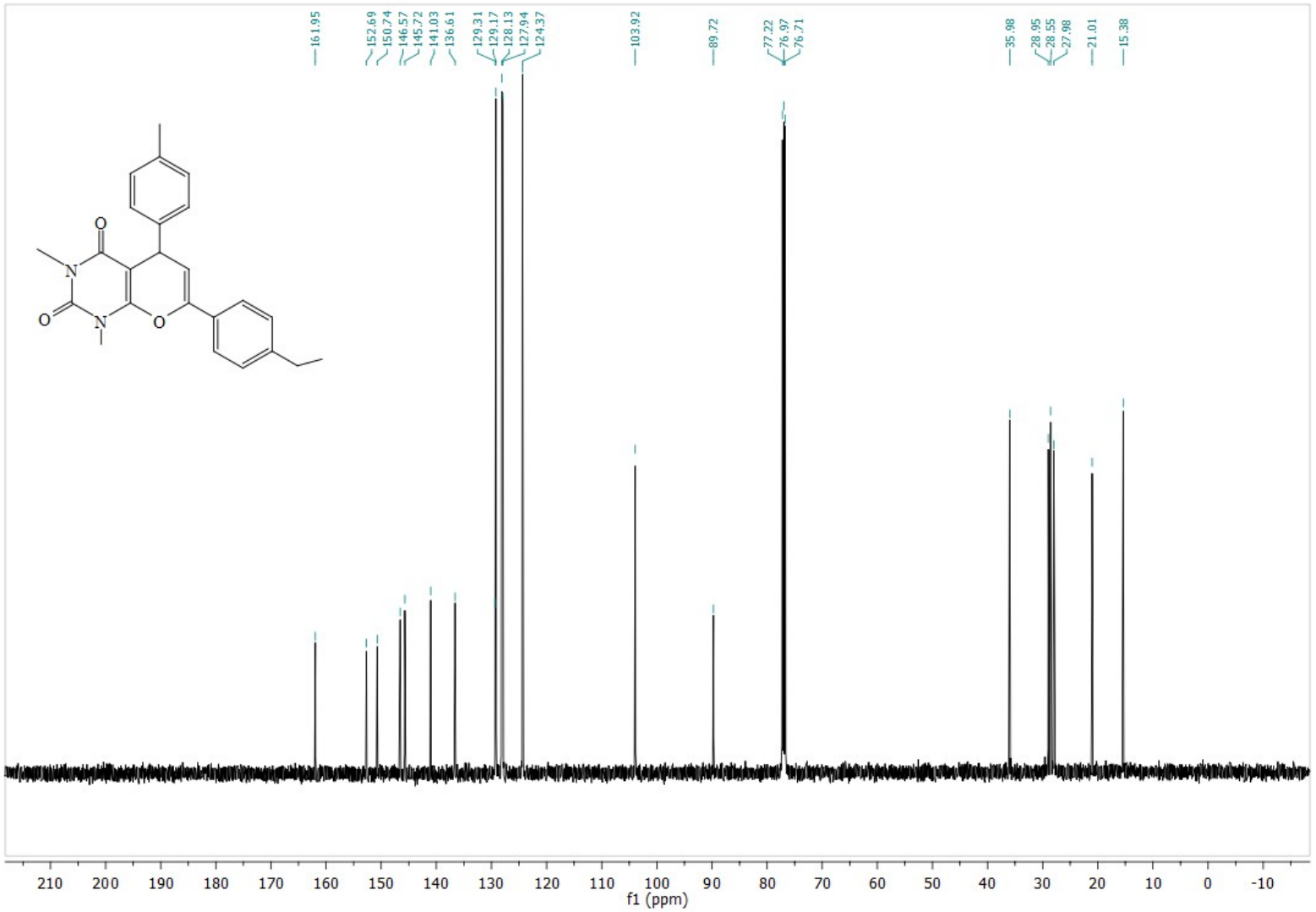
^{1}H NMR Spectrum of compound 4b



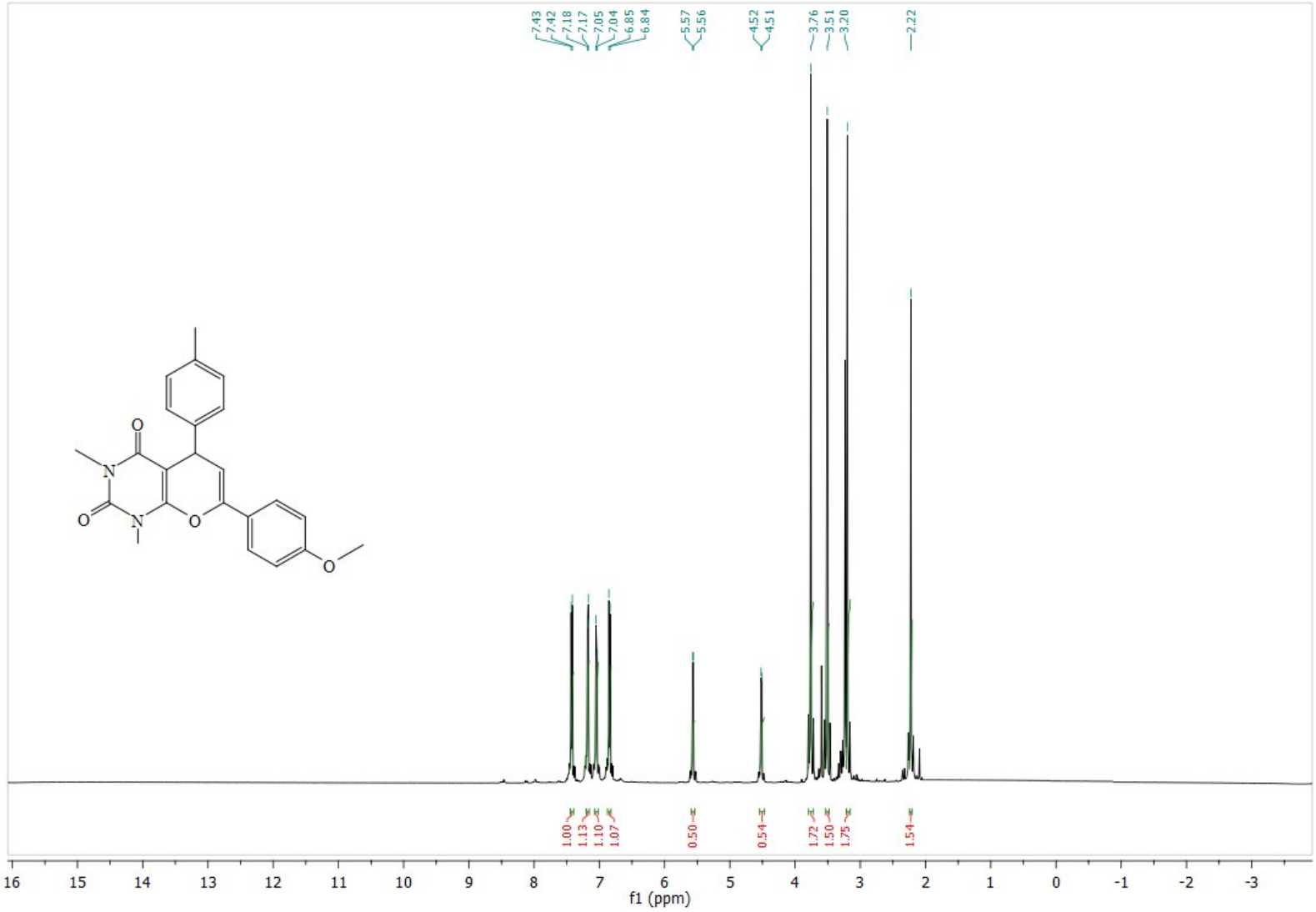
^{13}C NMR Spectrum of compound 4b



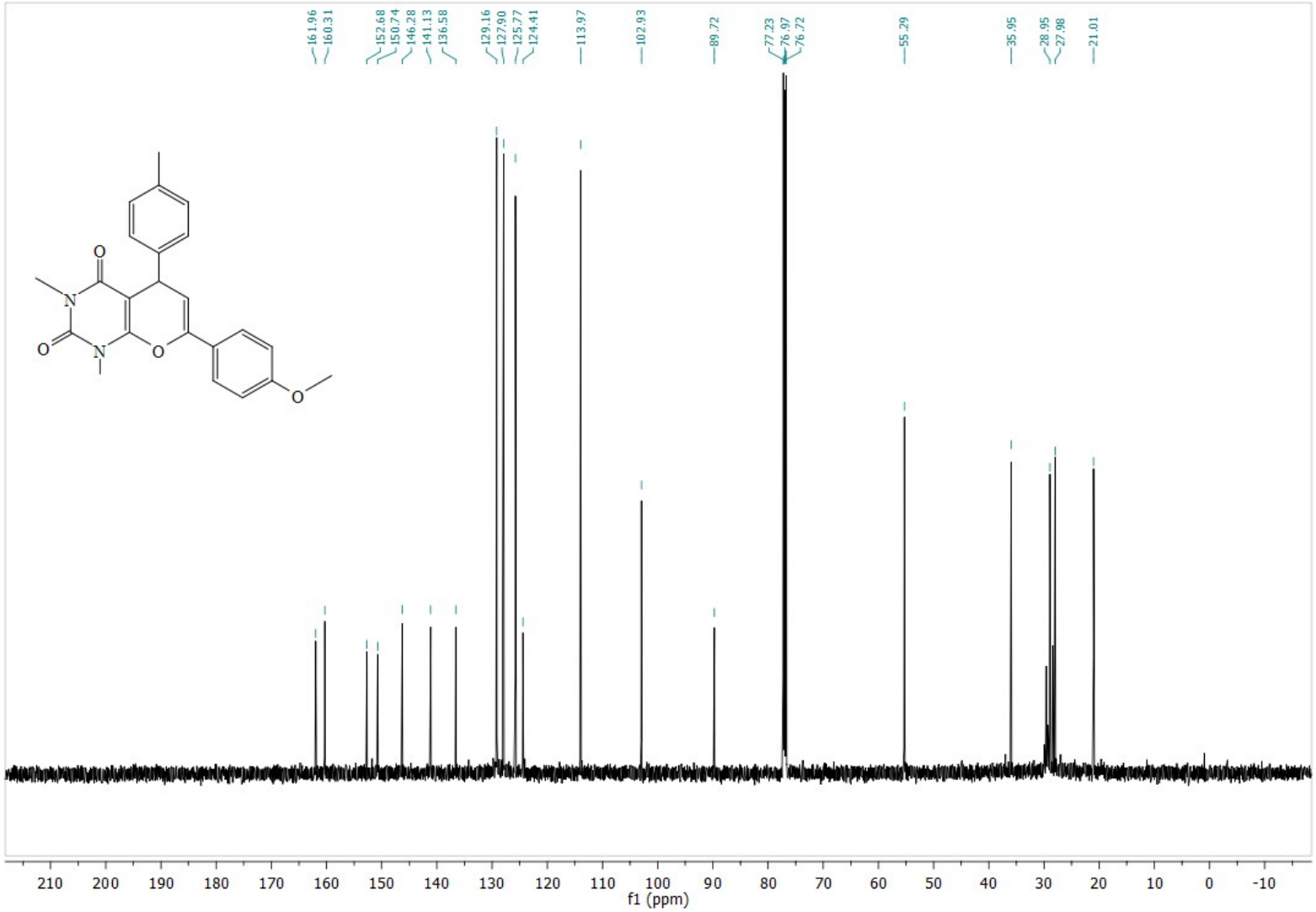
^{1}H NMR Spectrum of compound 4c



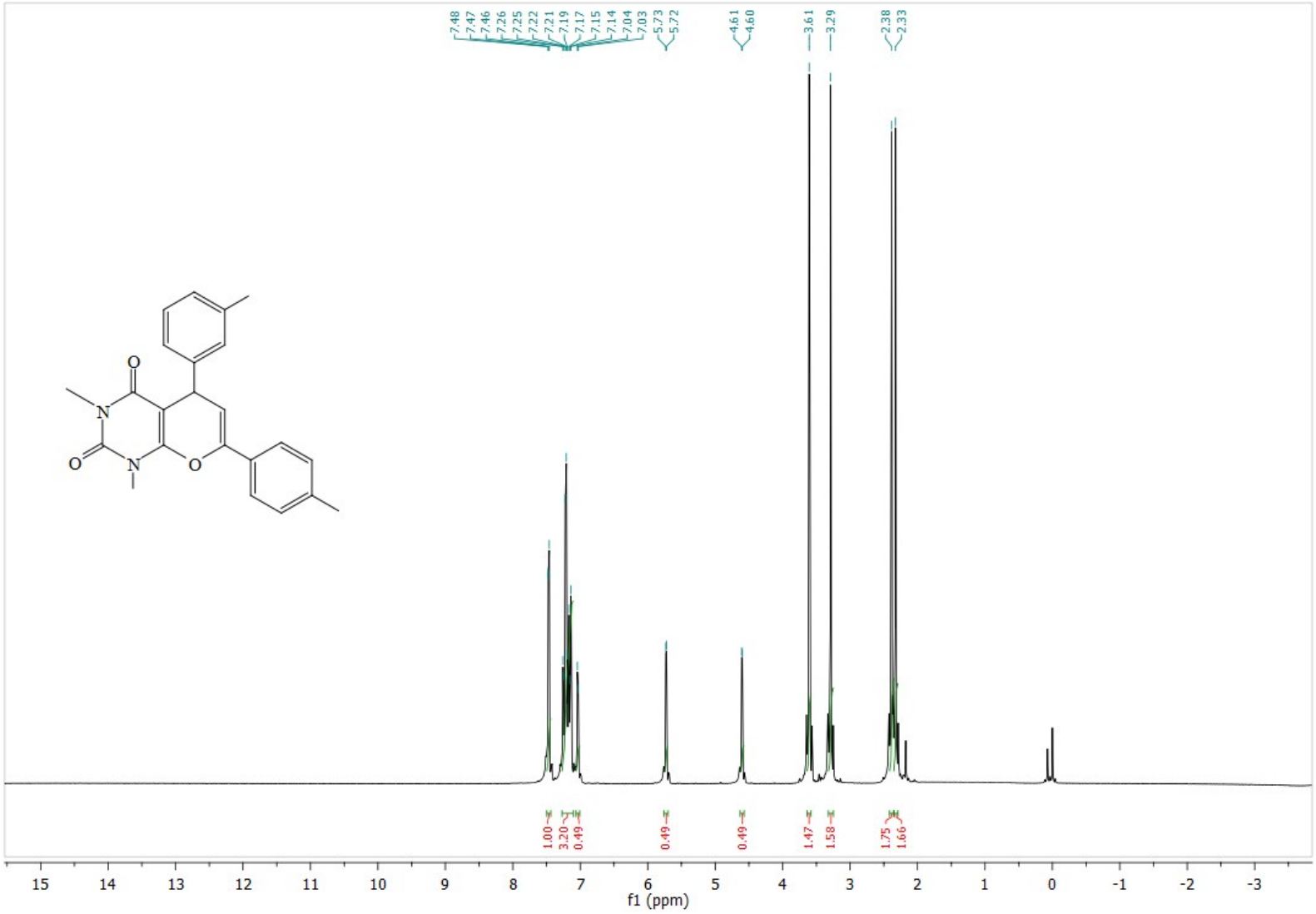
^{13}C NMR Spectrum of compound 4c



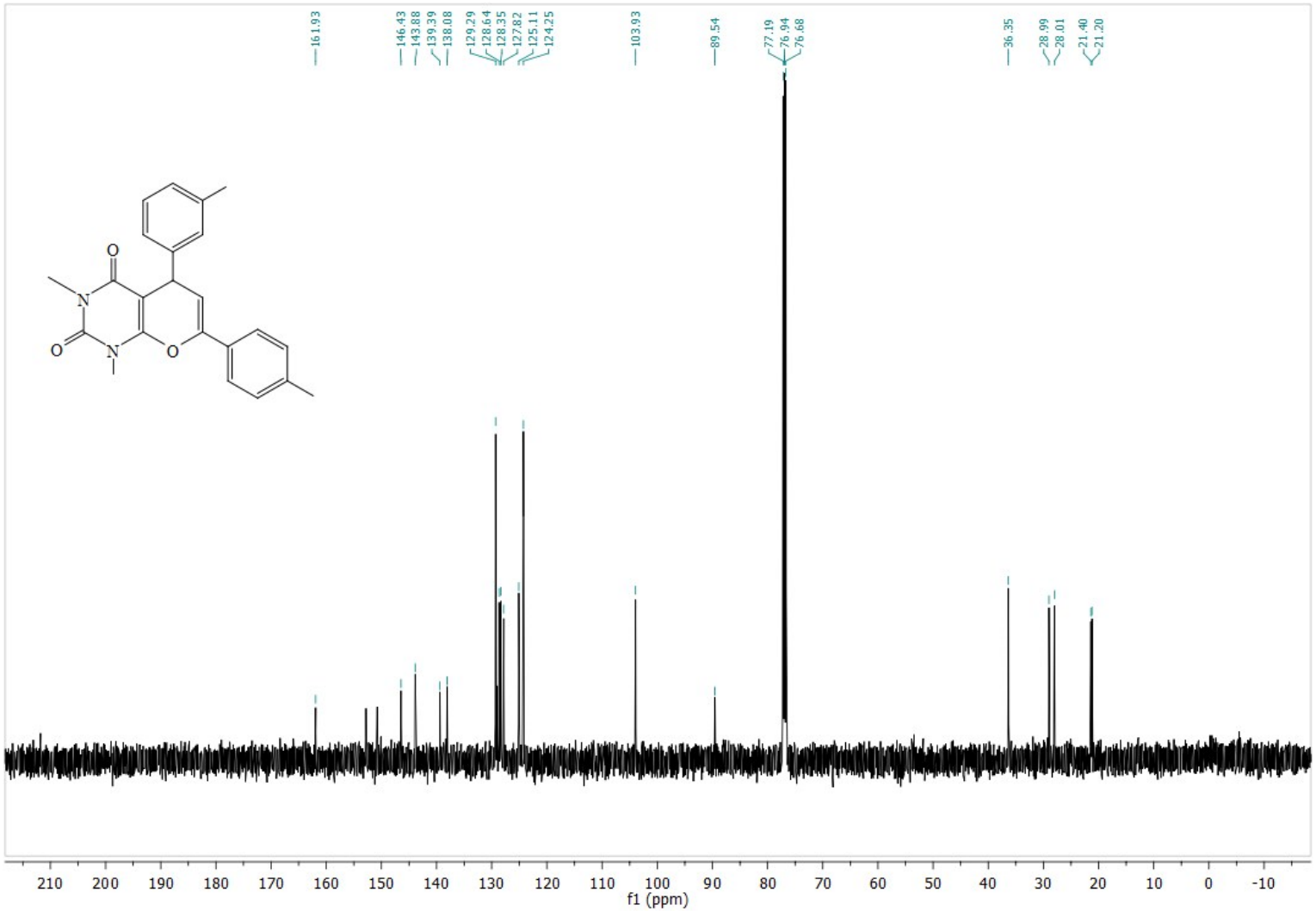
^{1}H NMR Spectrum of compound 4d



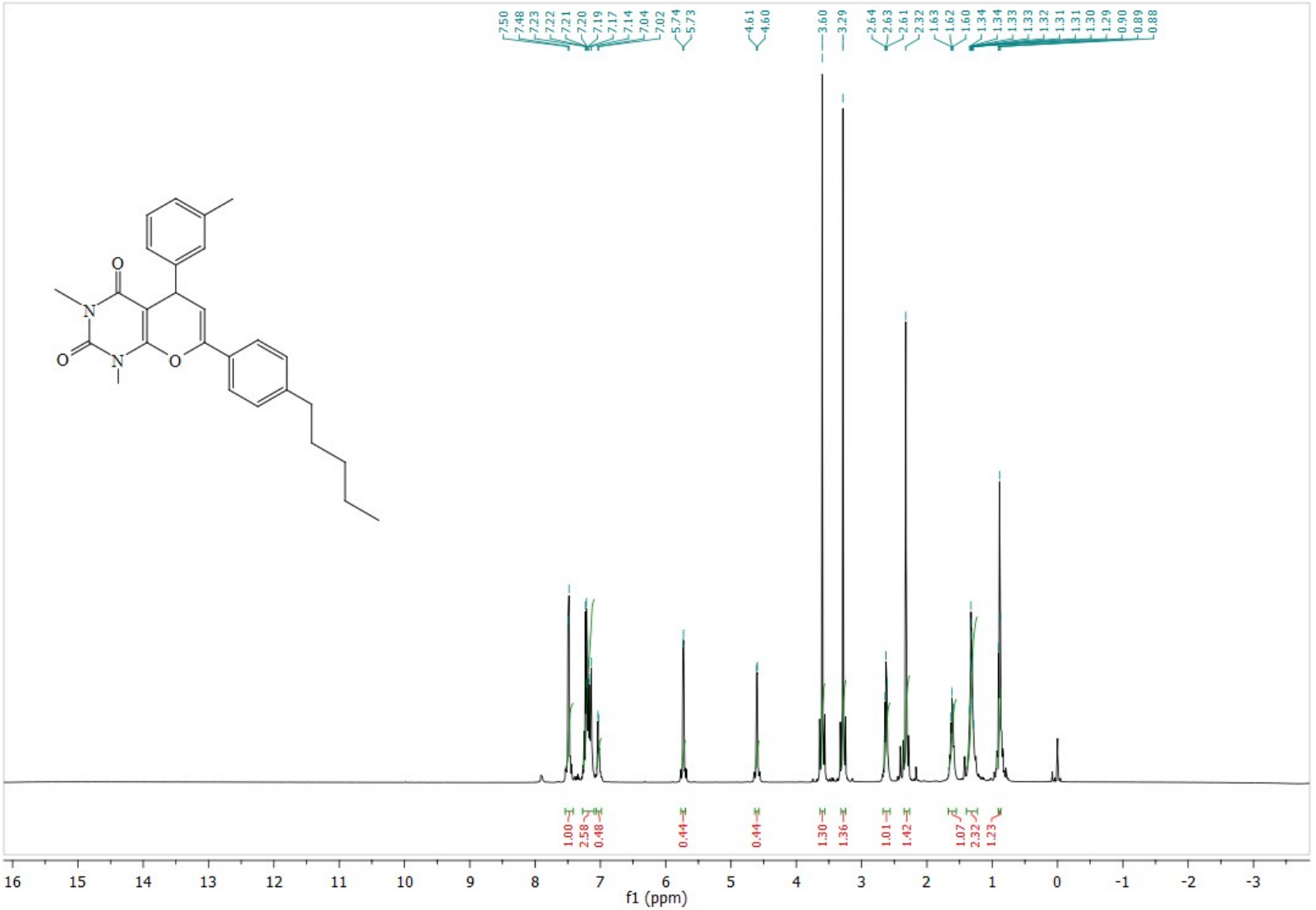
^{13}C NMR Spectrum of compound 4d



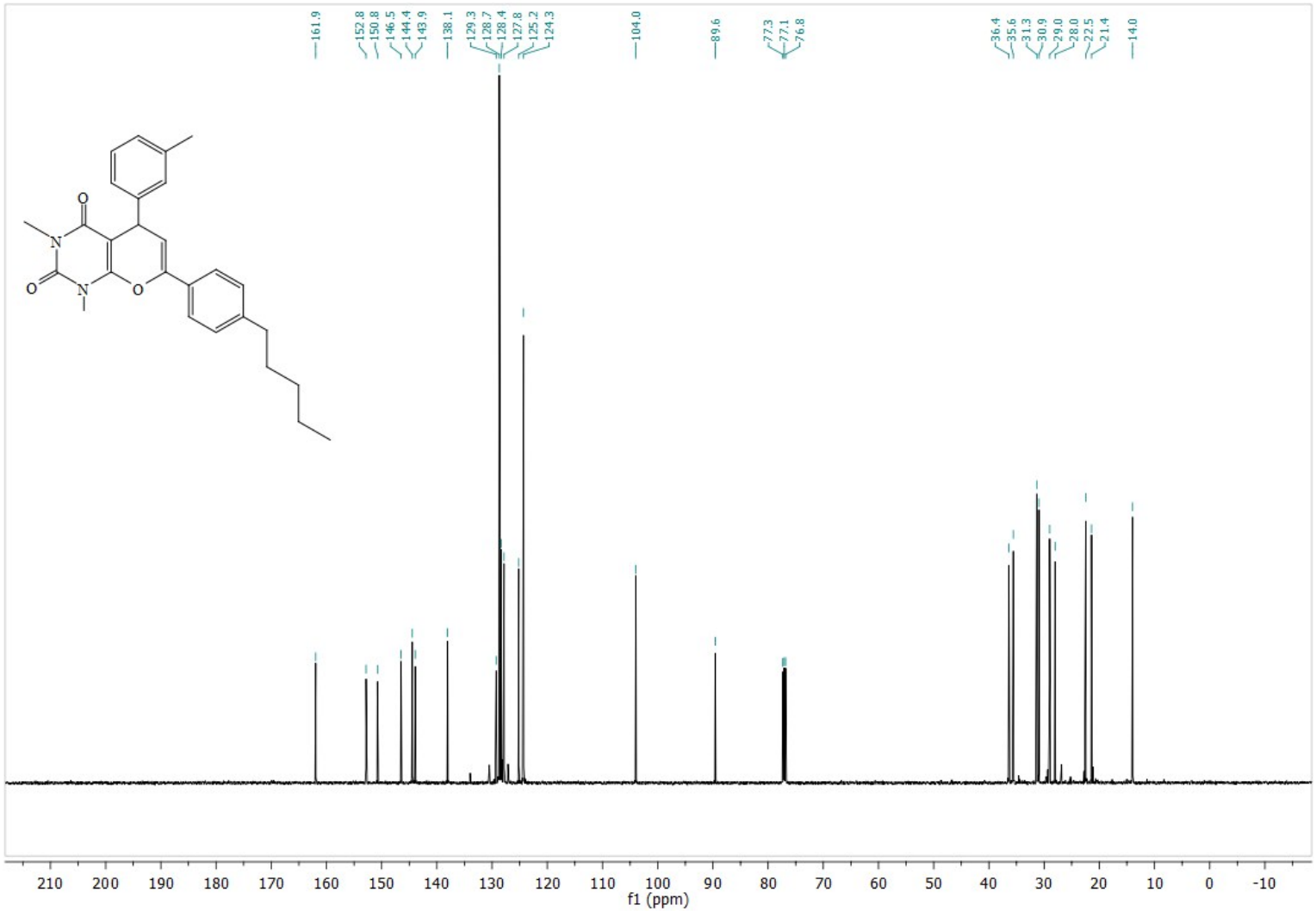
^{1}H NMR Spectrum of compound 4e



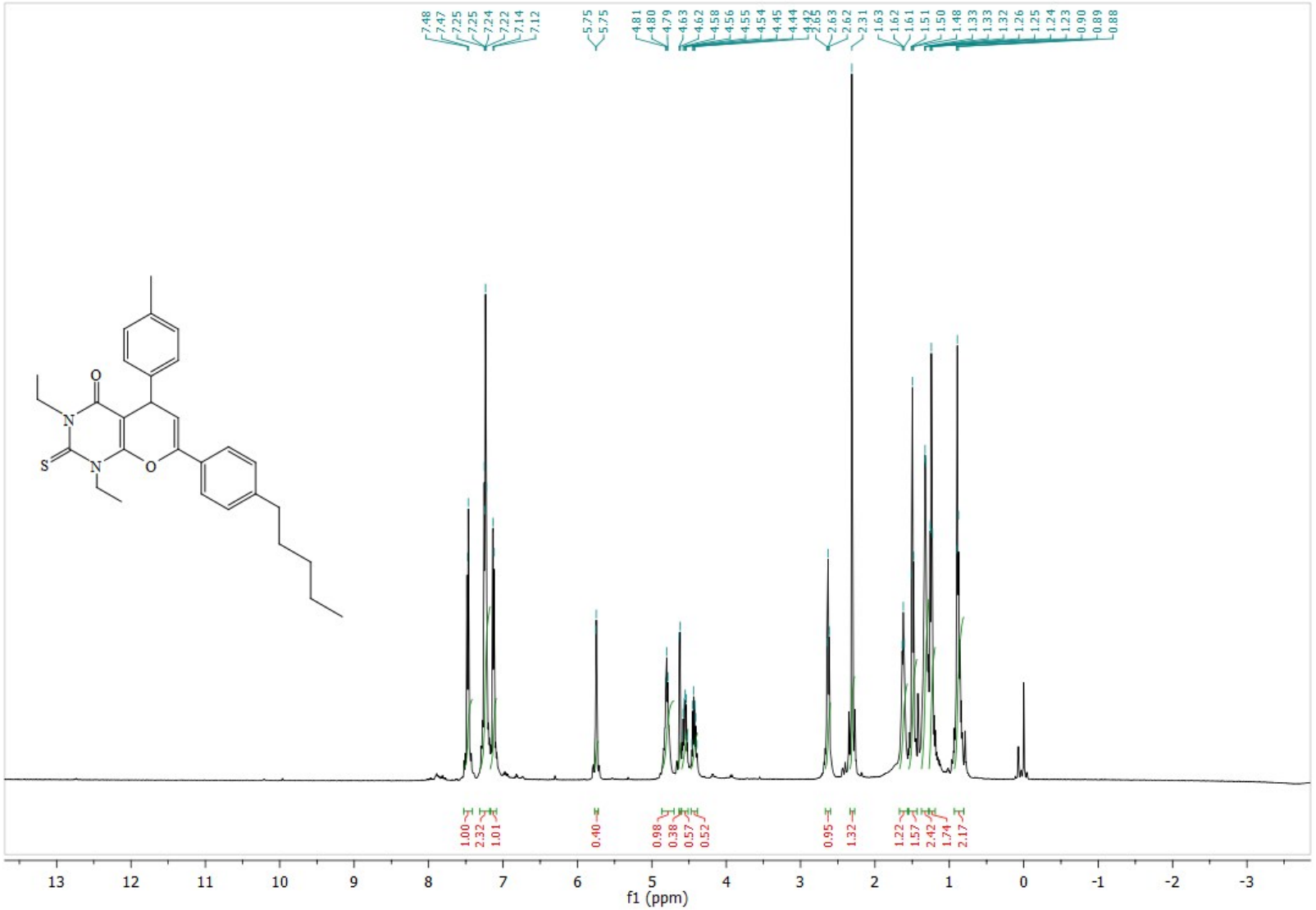
^{13}C NMR Spectrum of compound 4e



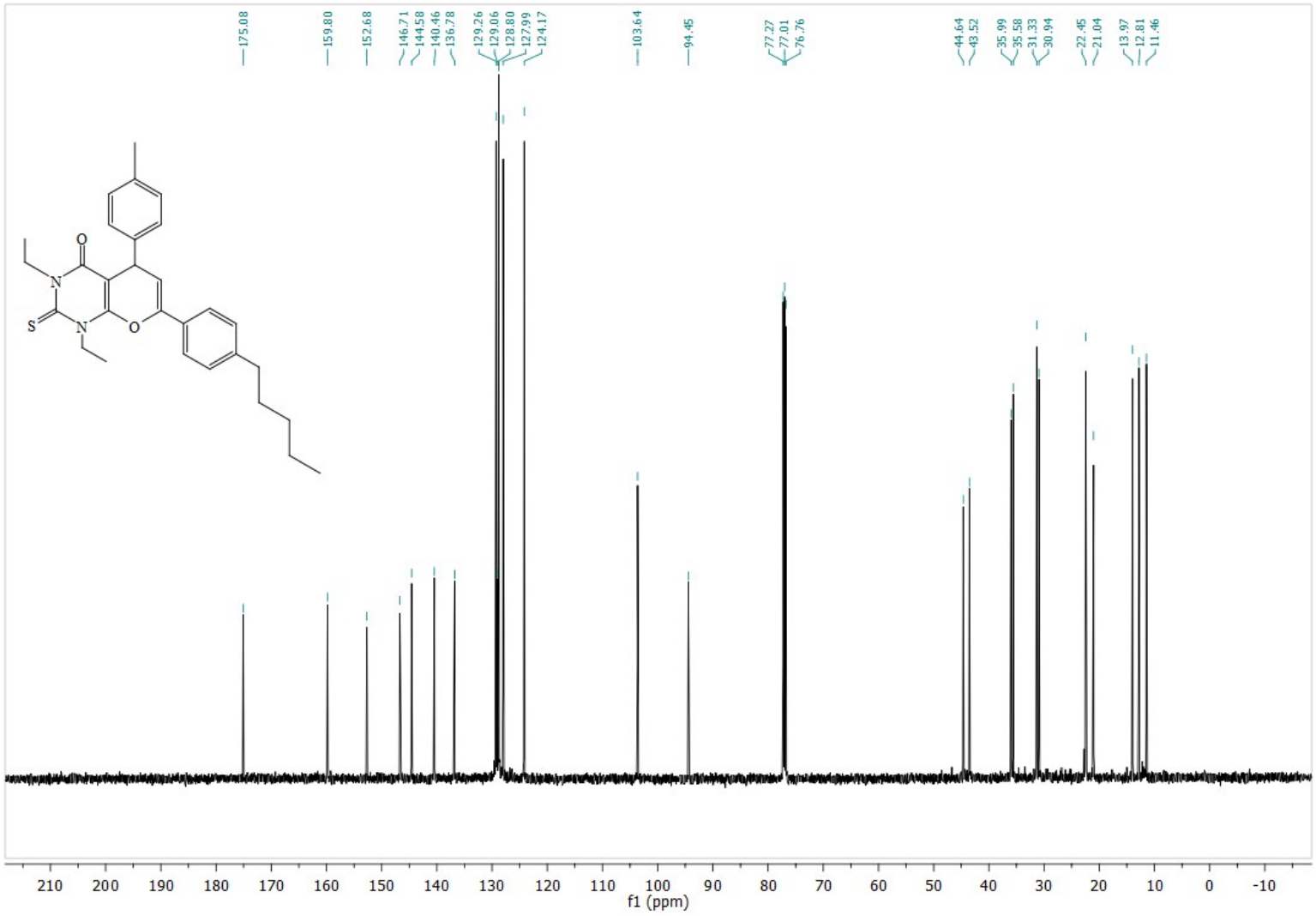
[1]H NMR Spectrum of compound 4f



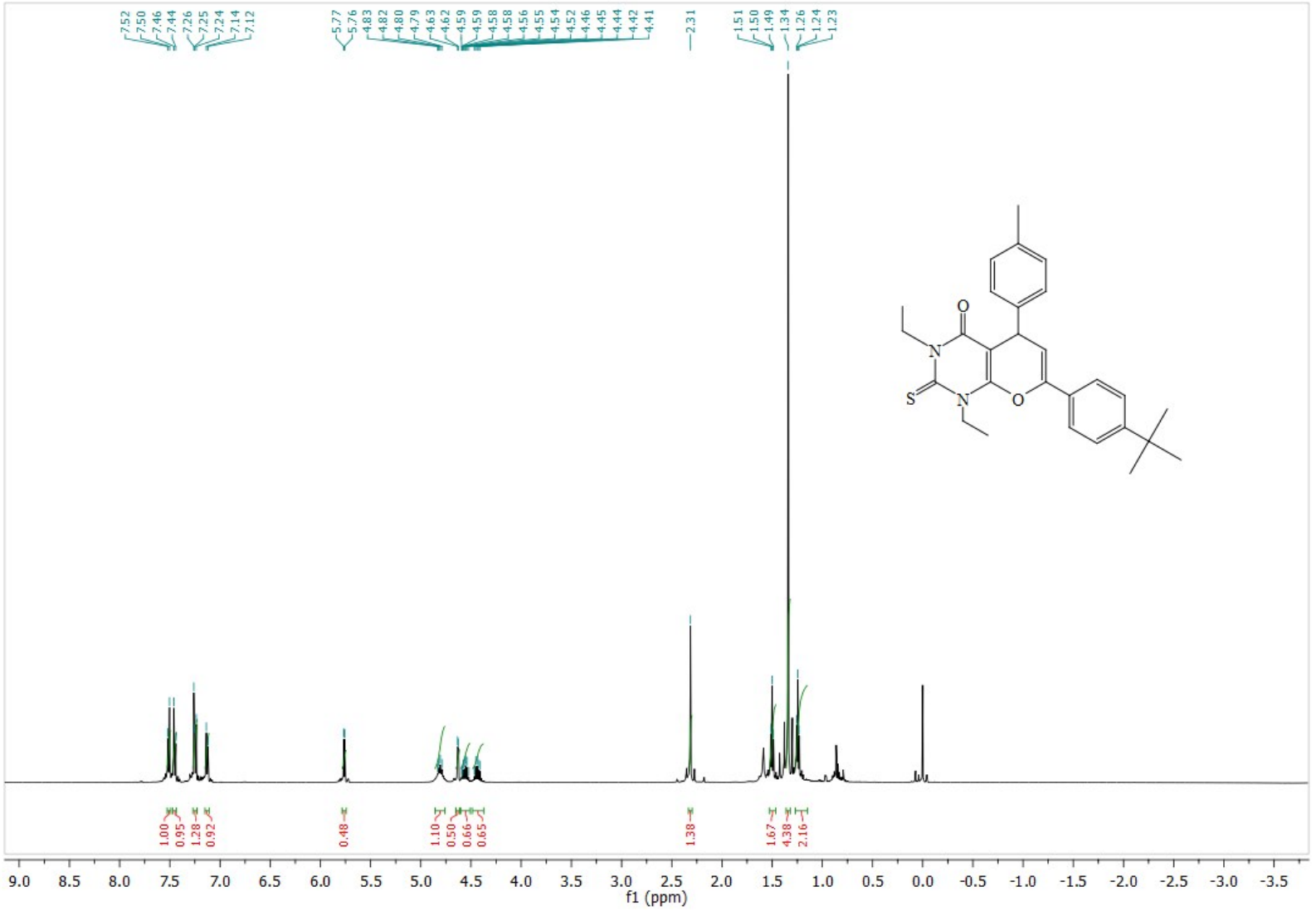
^{13}C NMR Spectrum of compound 4f



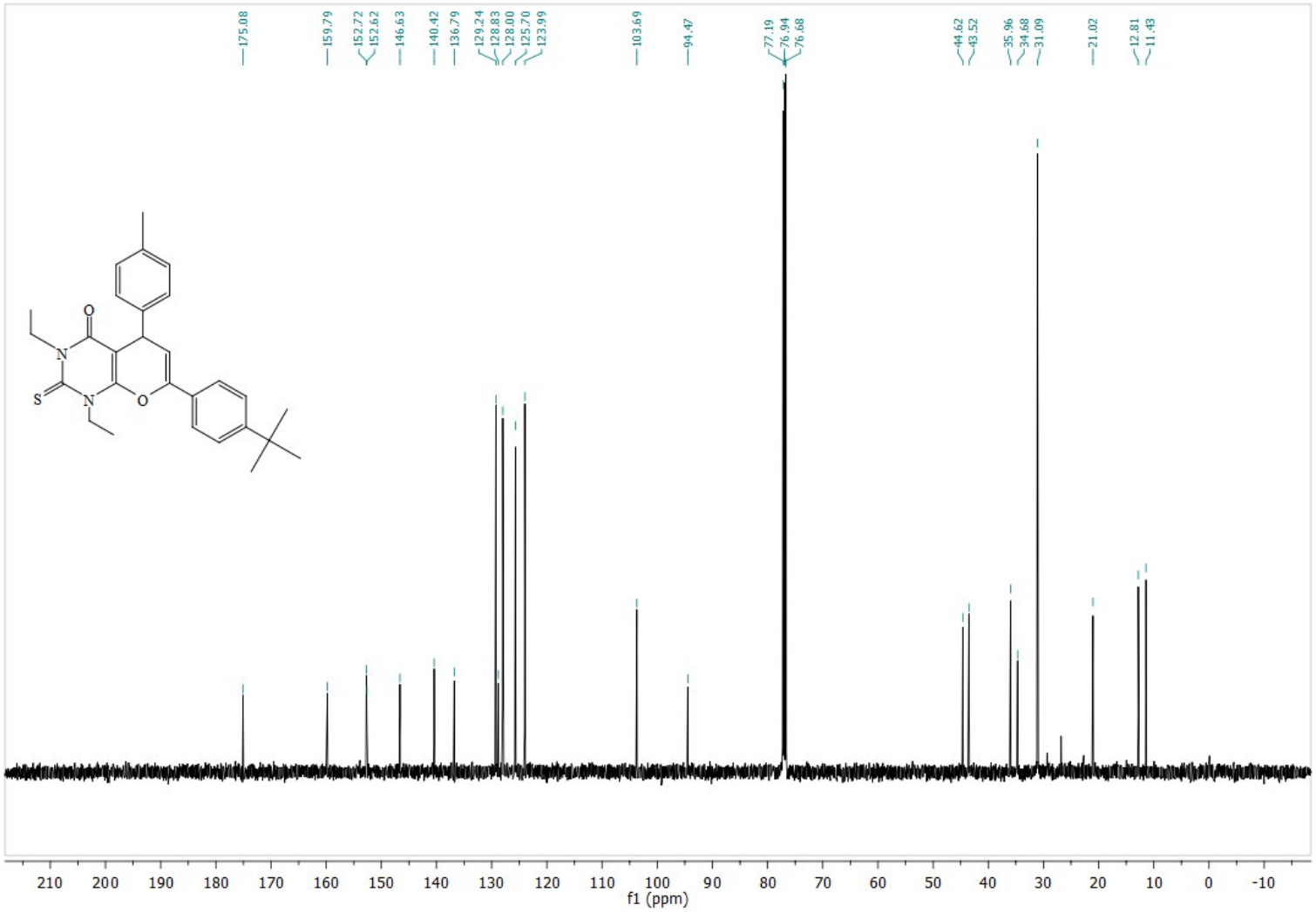
[1]H NMR Spectrum of compound 4g



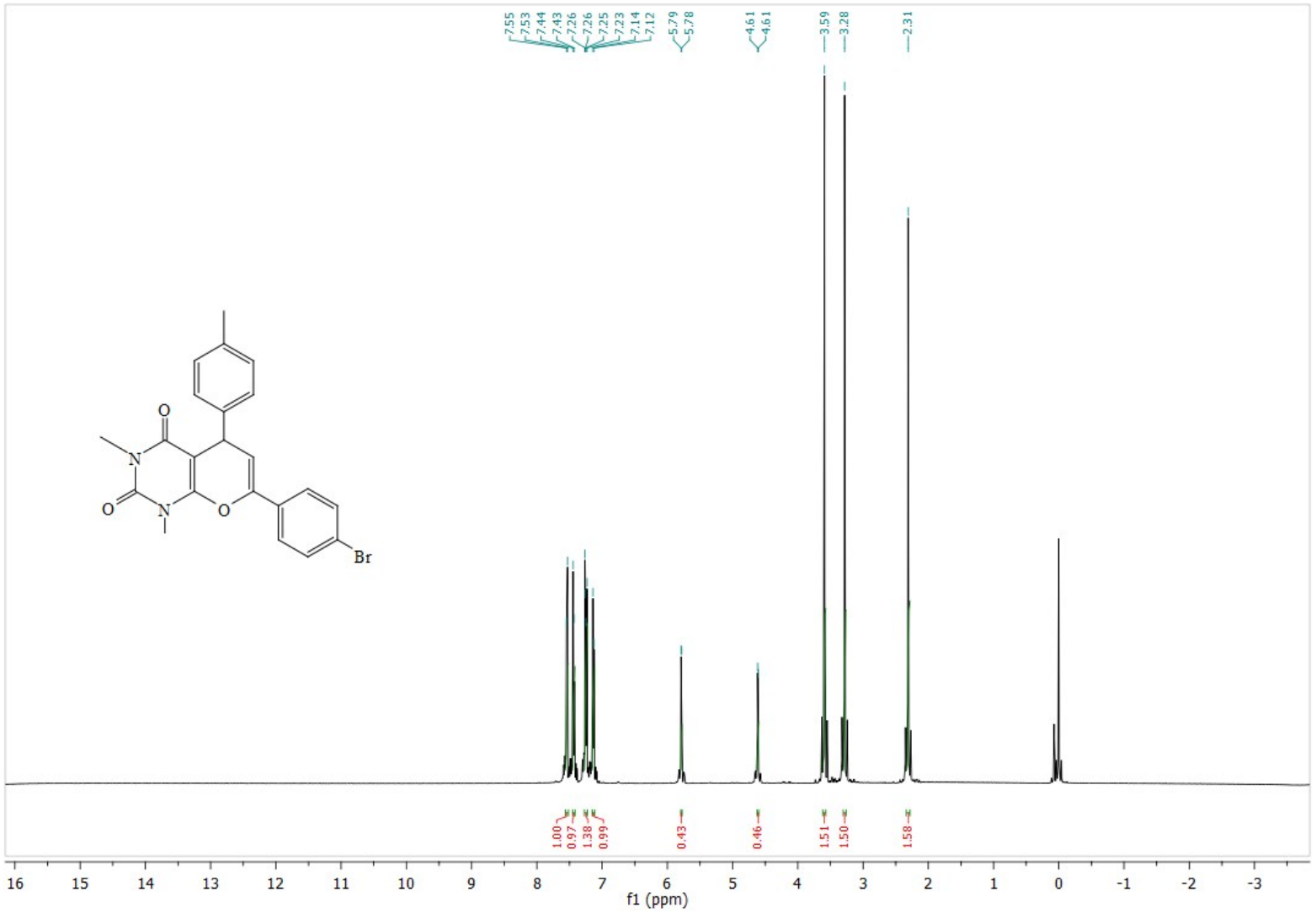
^{13}C NMR Spectrum of compound 4g



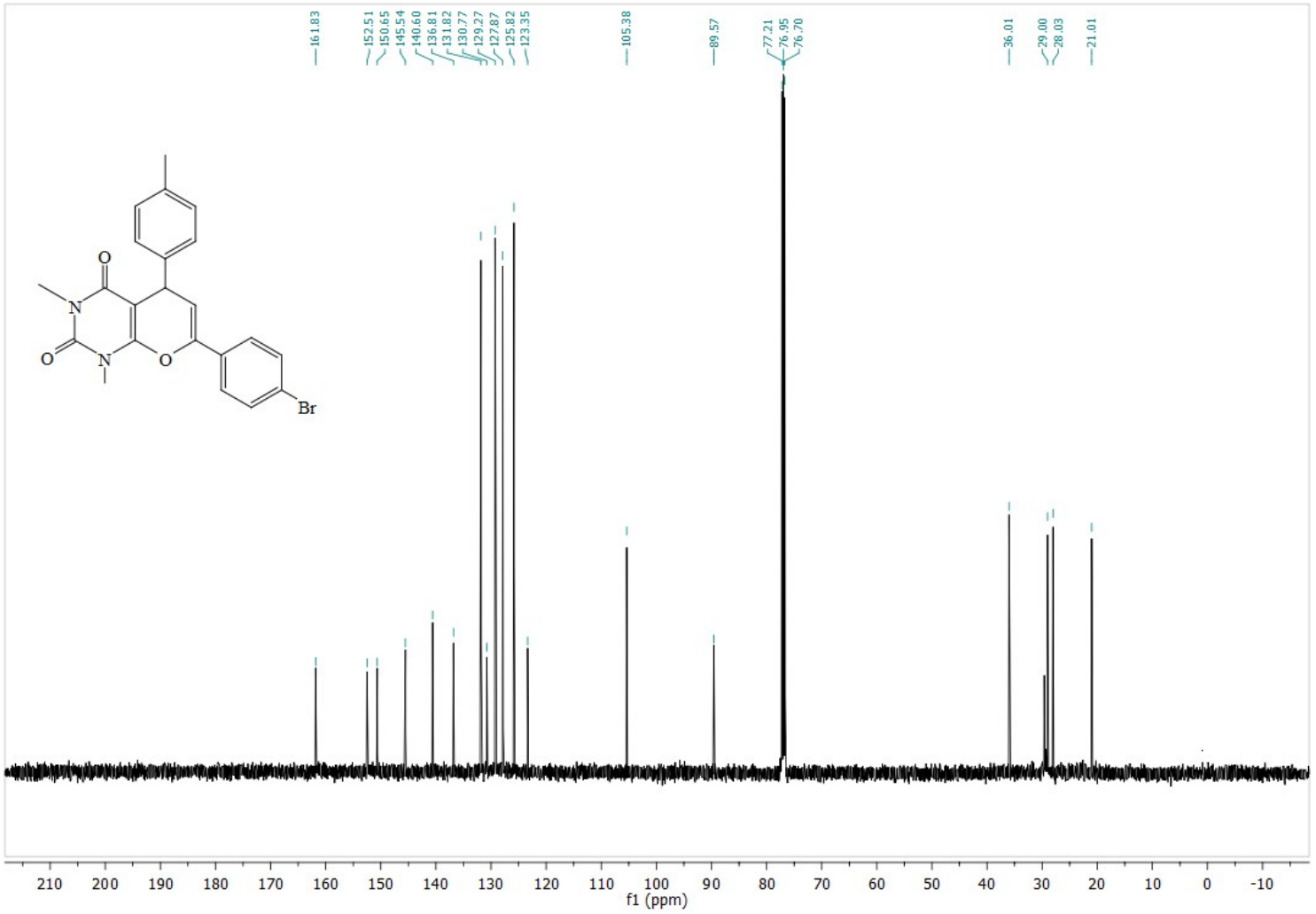
^{1}H NMR Spectrum of compound 4h



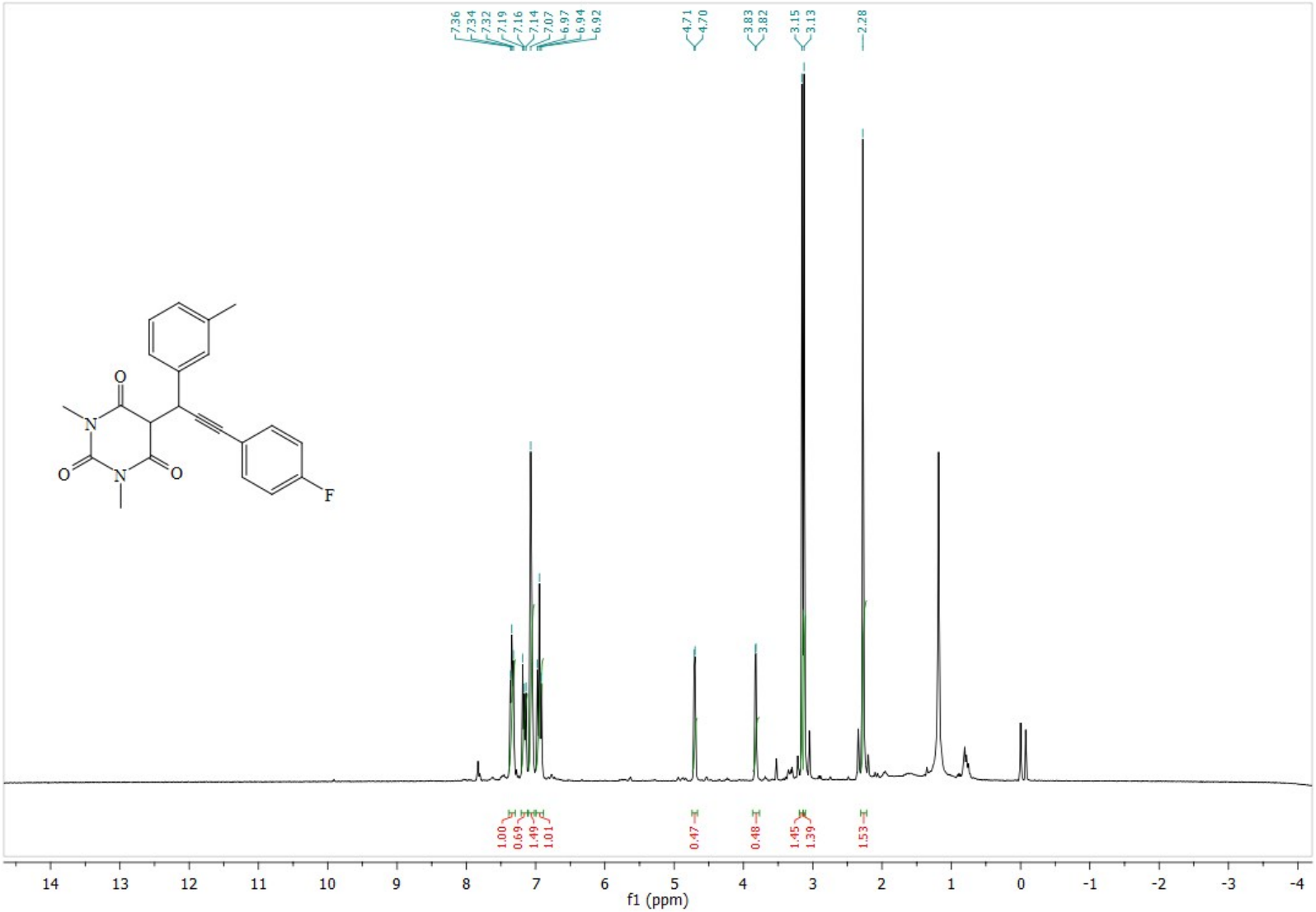
^{13}C NMR Spectrum of compound 4h



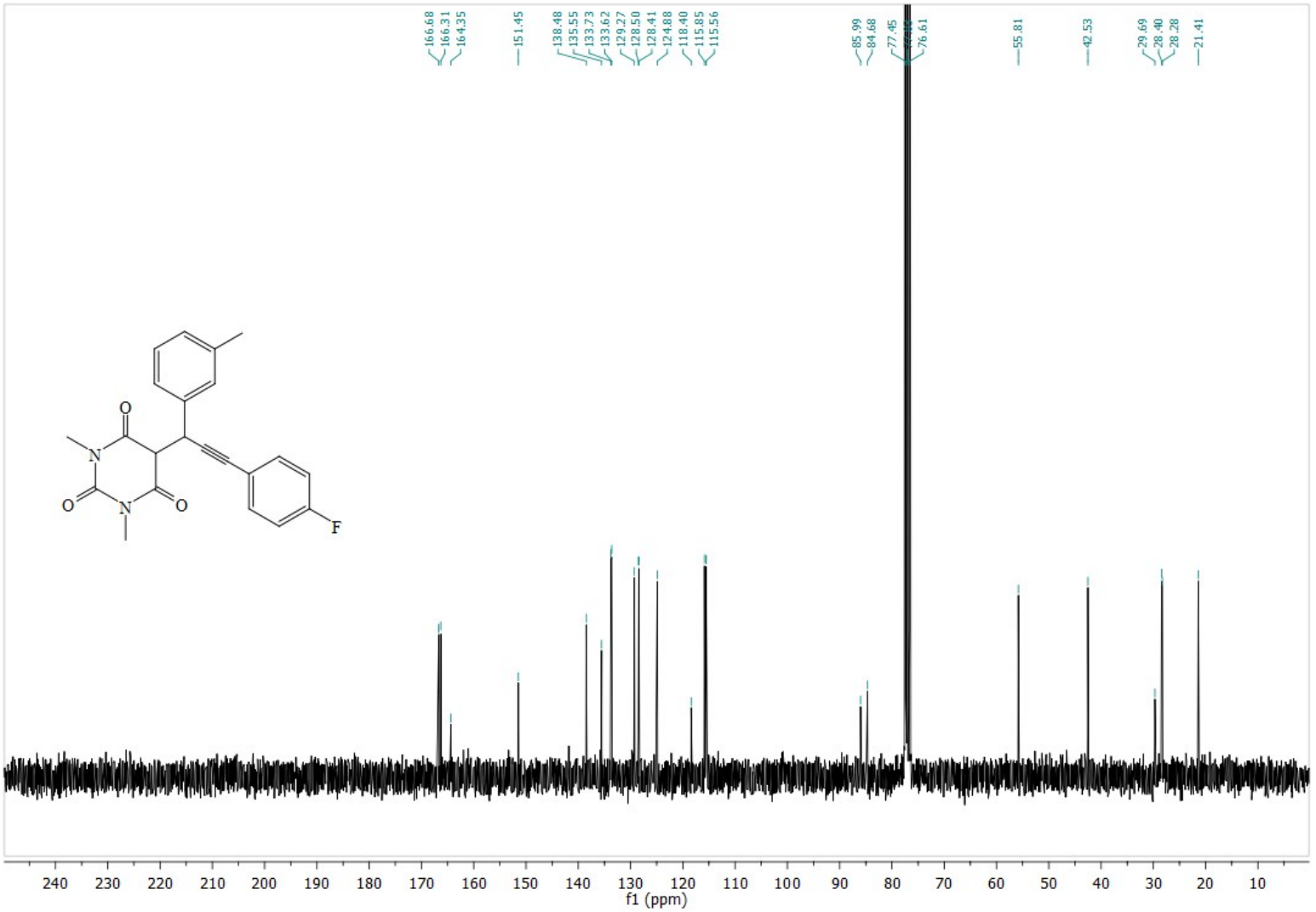
^{1}H NMR Spectrum of compound 4i



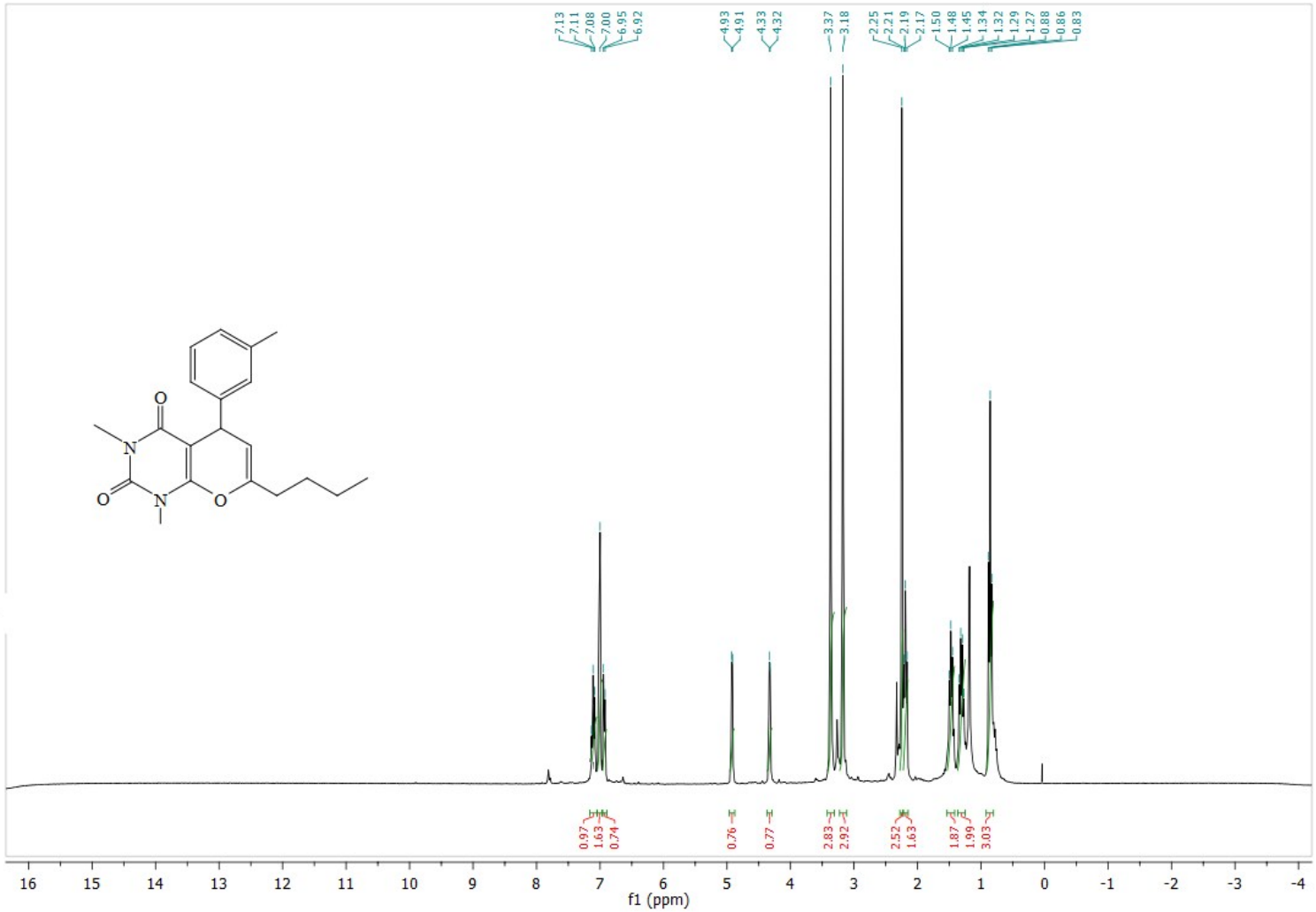
^{13}C NMR Spectrum of compound 4i



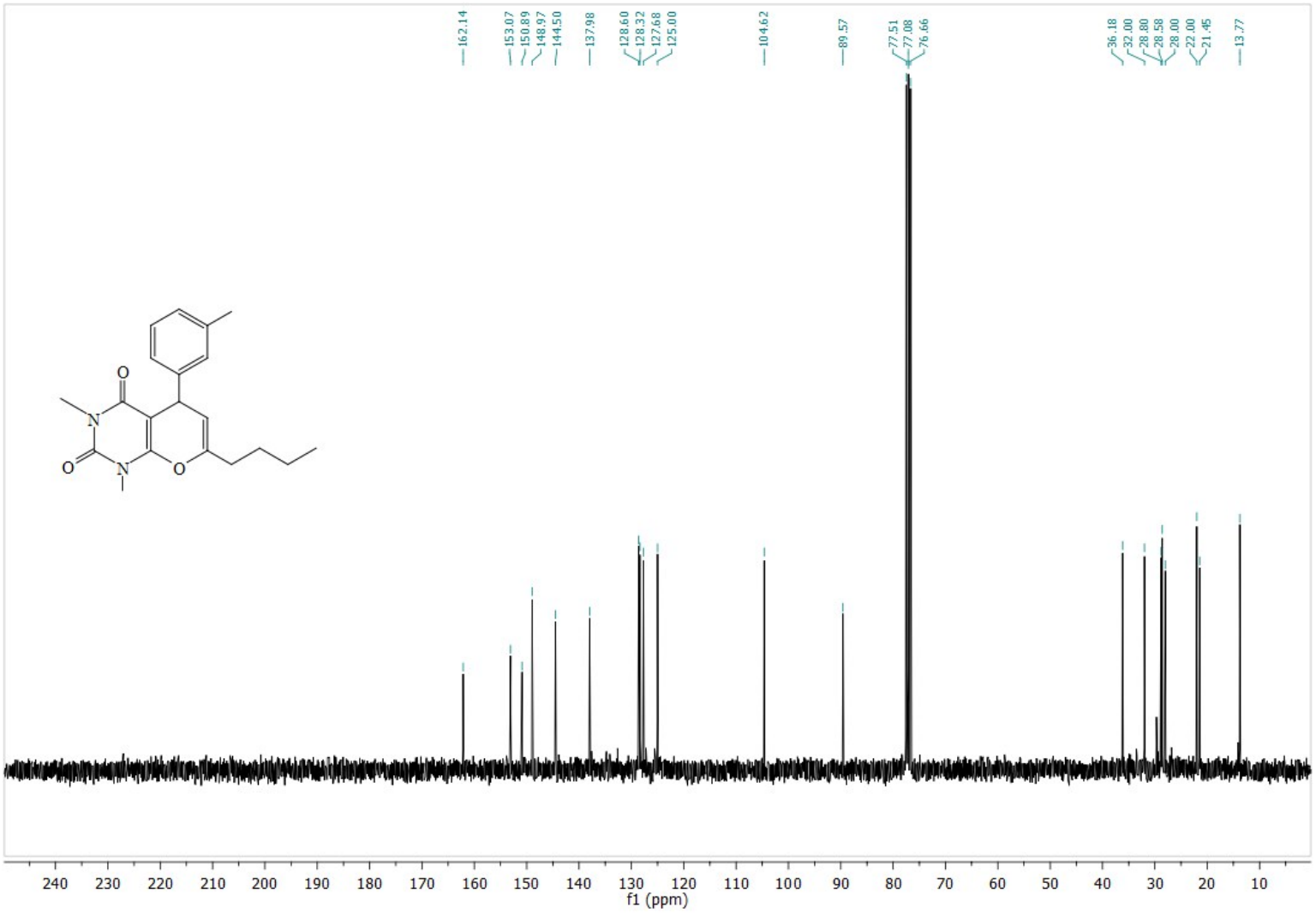
^{1}H NMR Spectrum of compound 4ii'



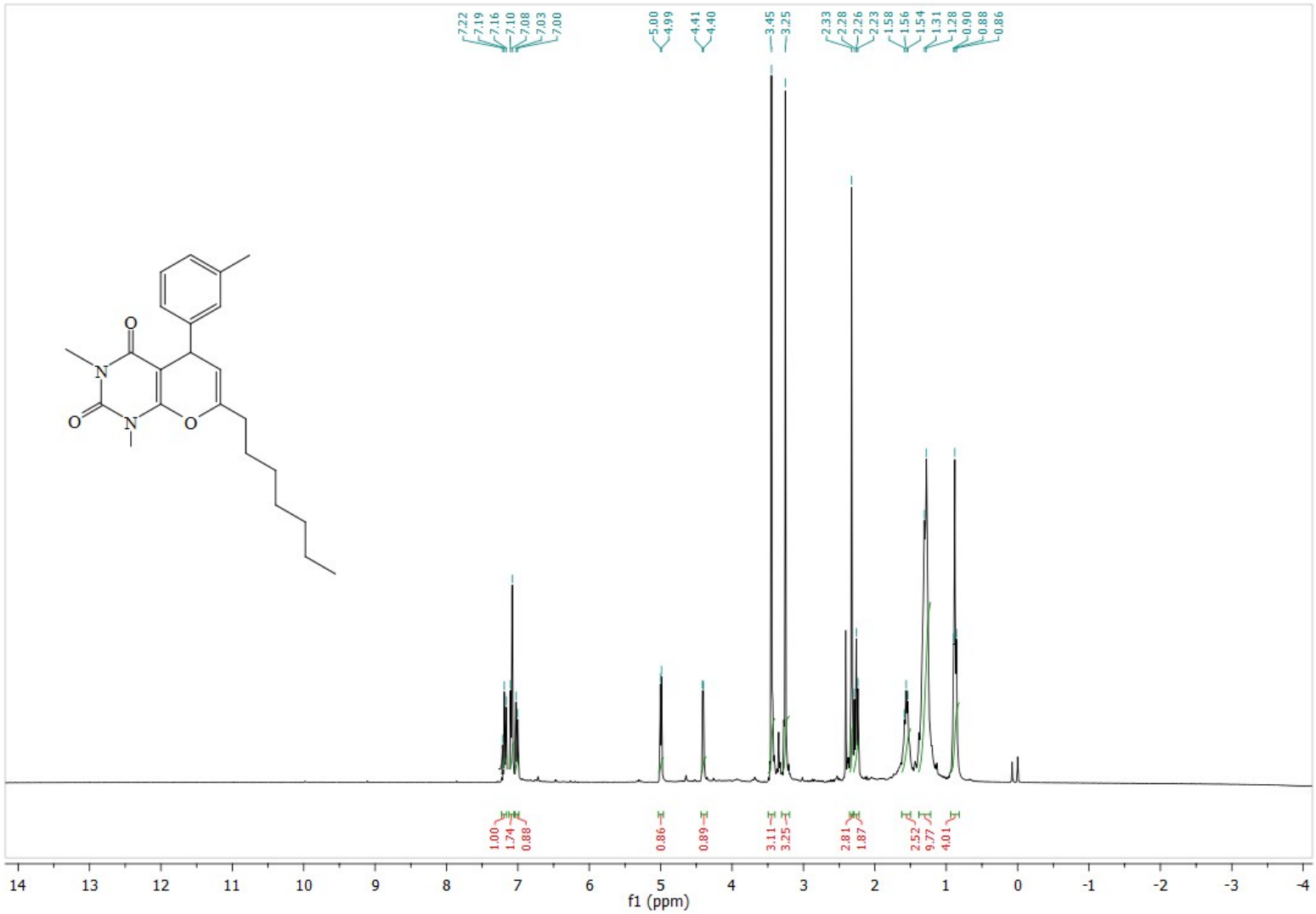
^{13}C NMR Spectrum of compound 4ii'



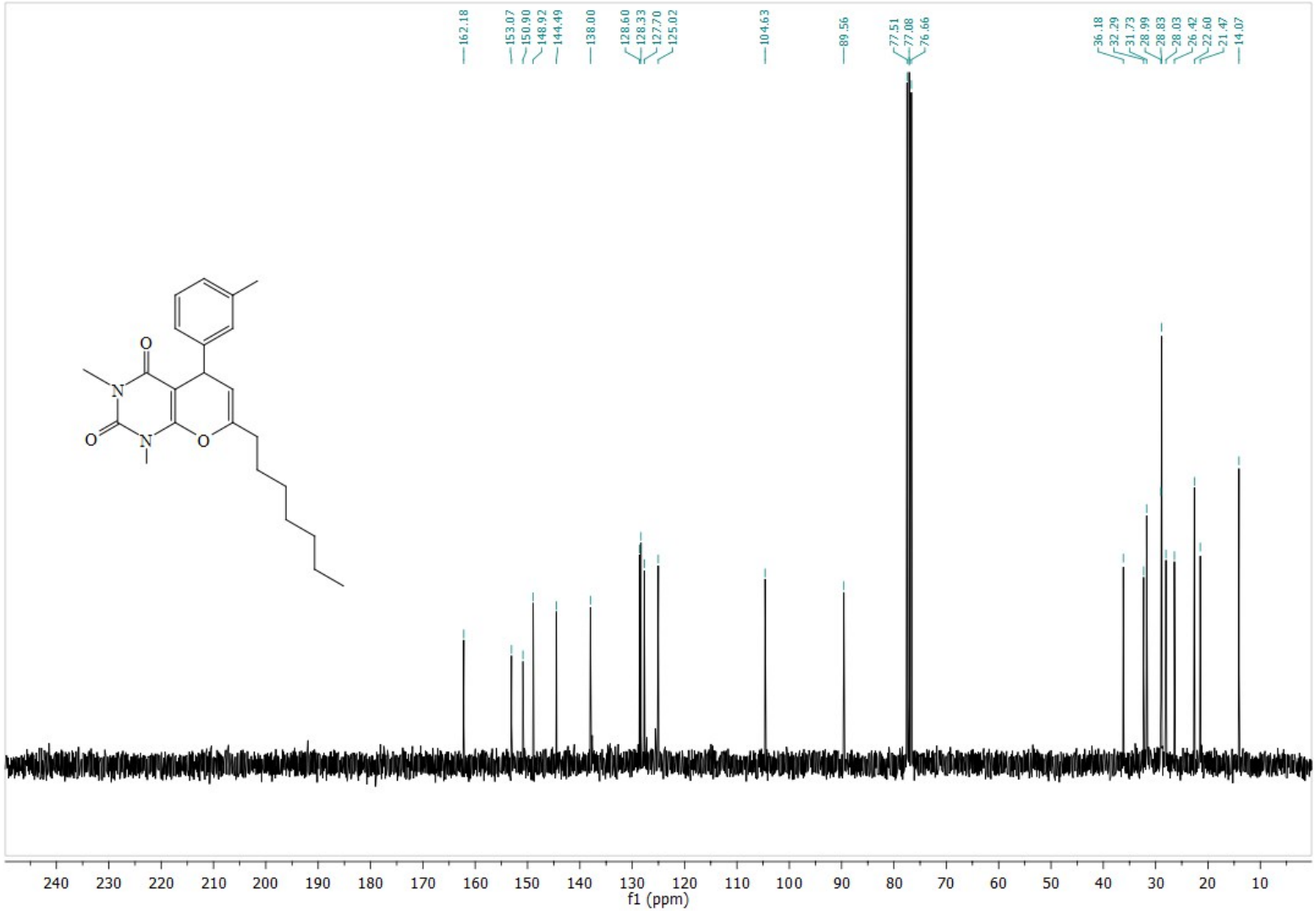
^{1}H NMR Spectrum of compound 4j



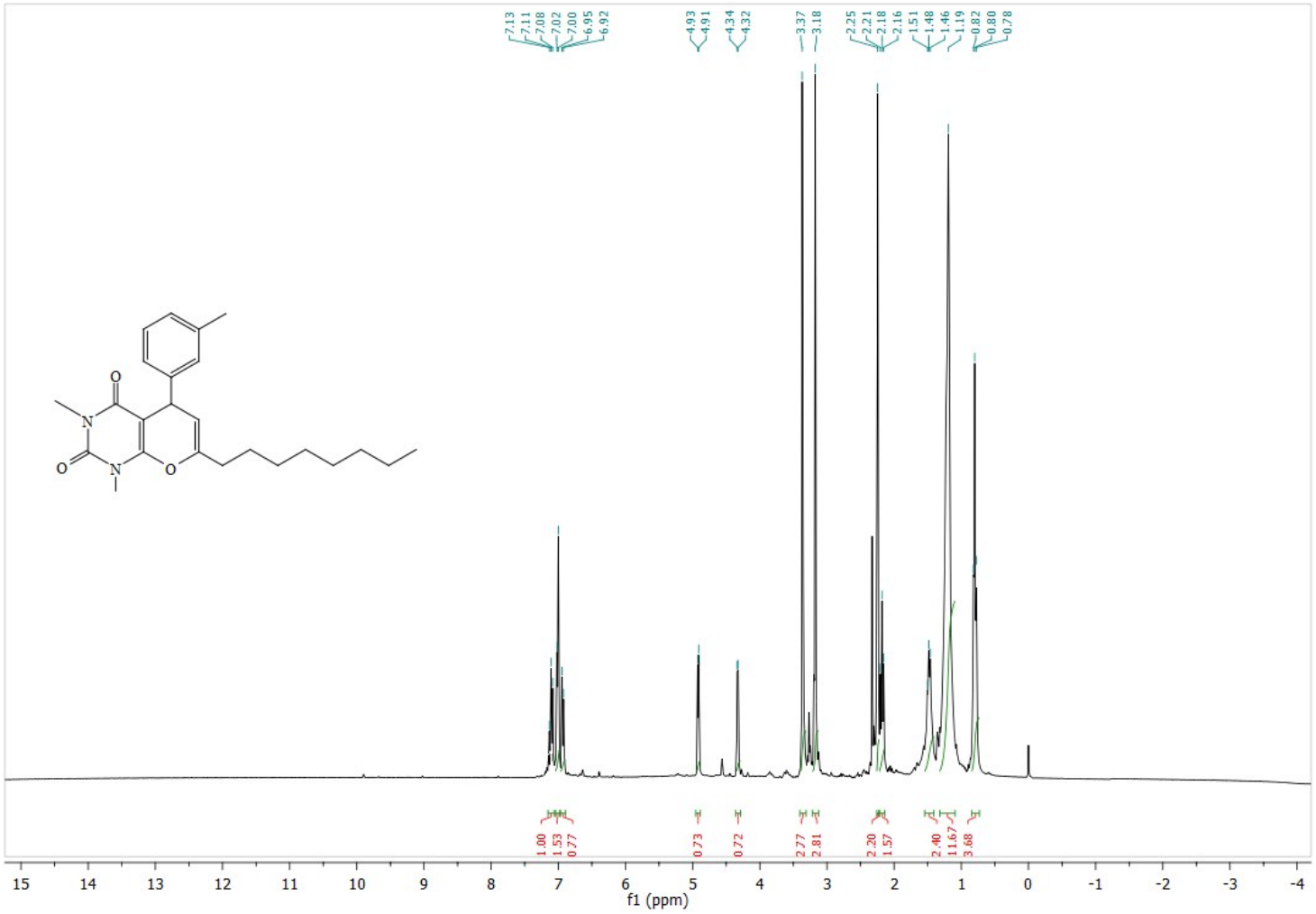
^{13}C NMR Spectrum of compound 4j



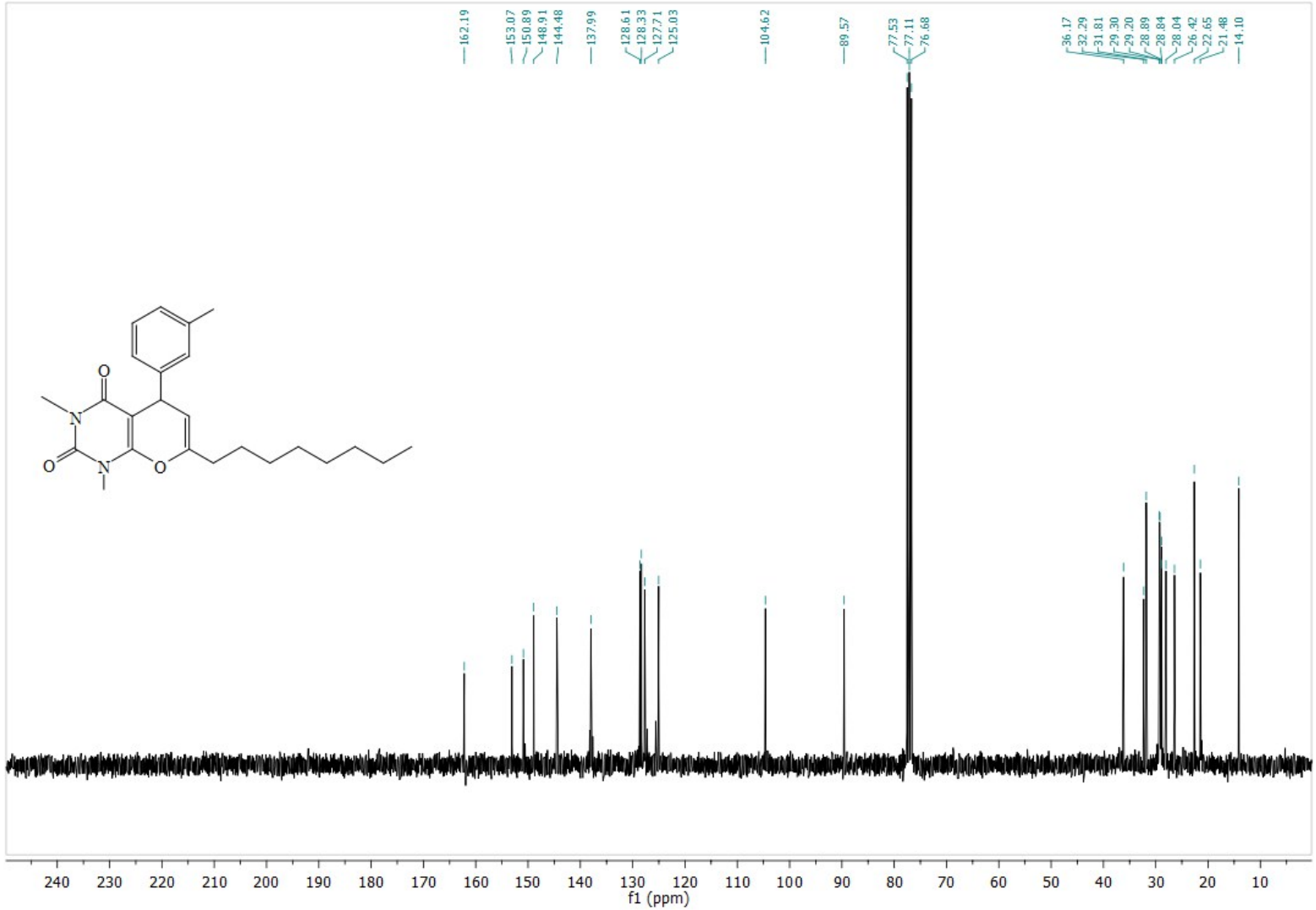
^{1}H NMR Spectrum of compound 4k



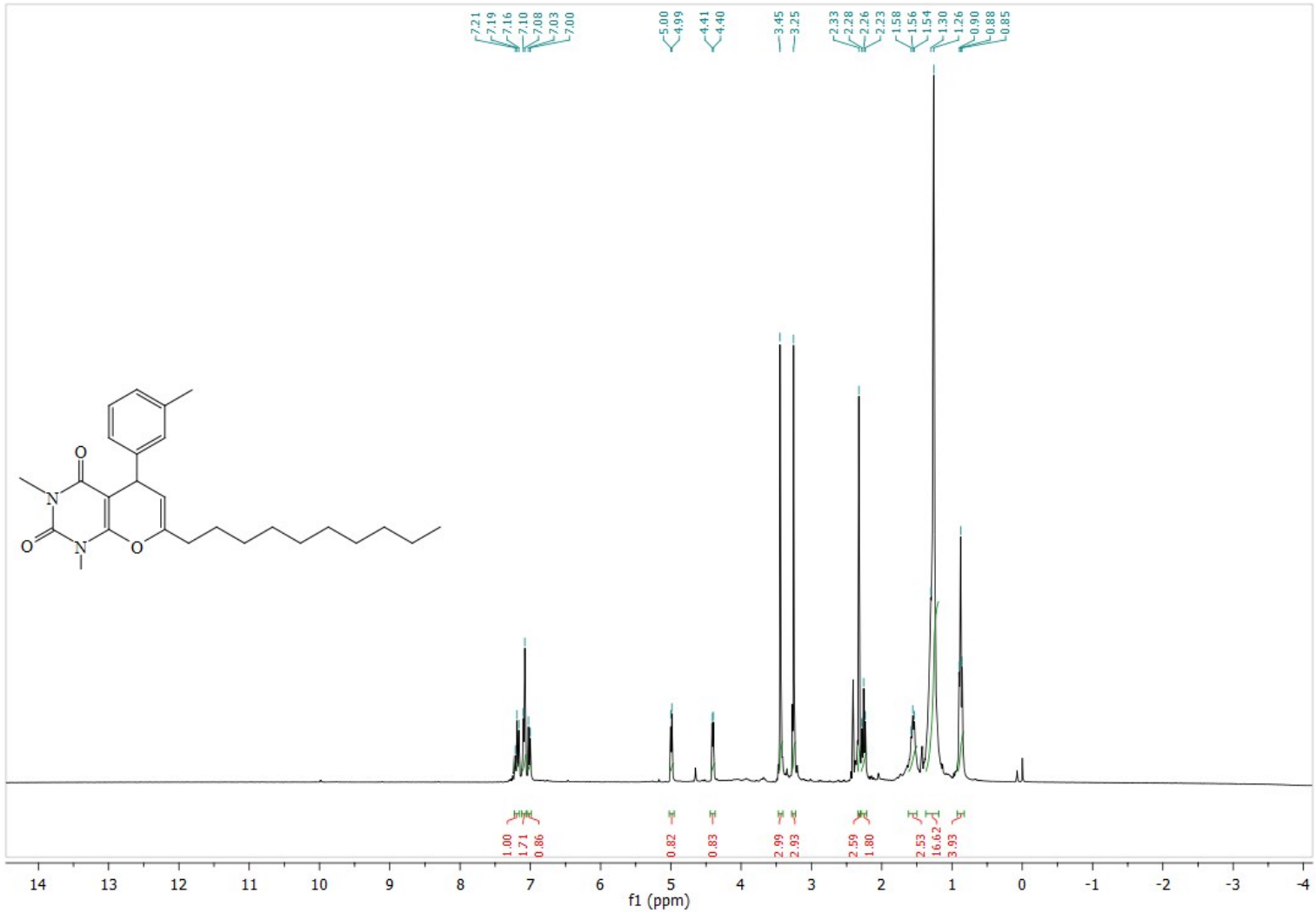
^{13}C NMR Spectrum of compound 4k



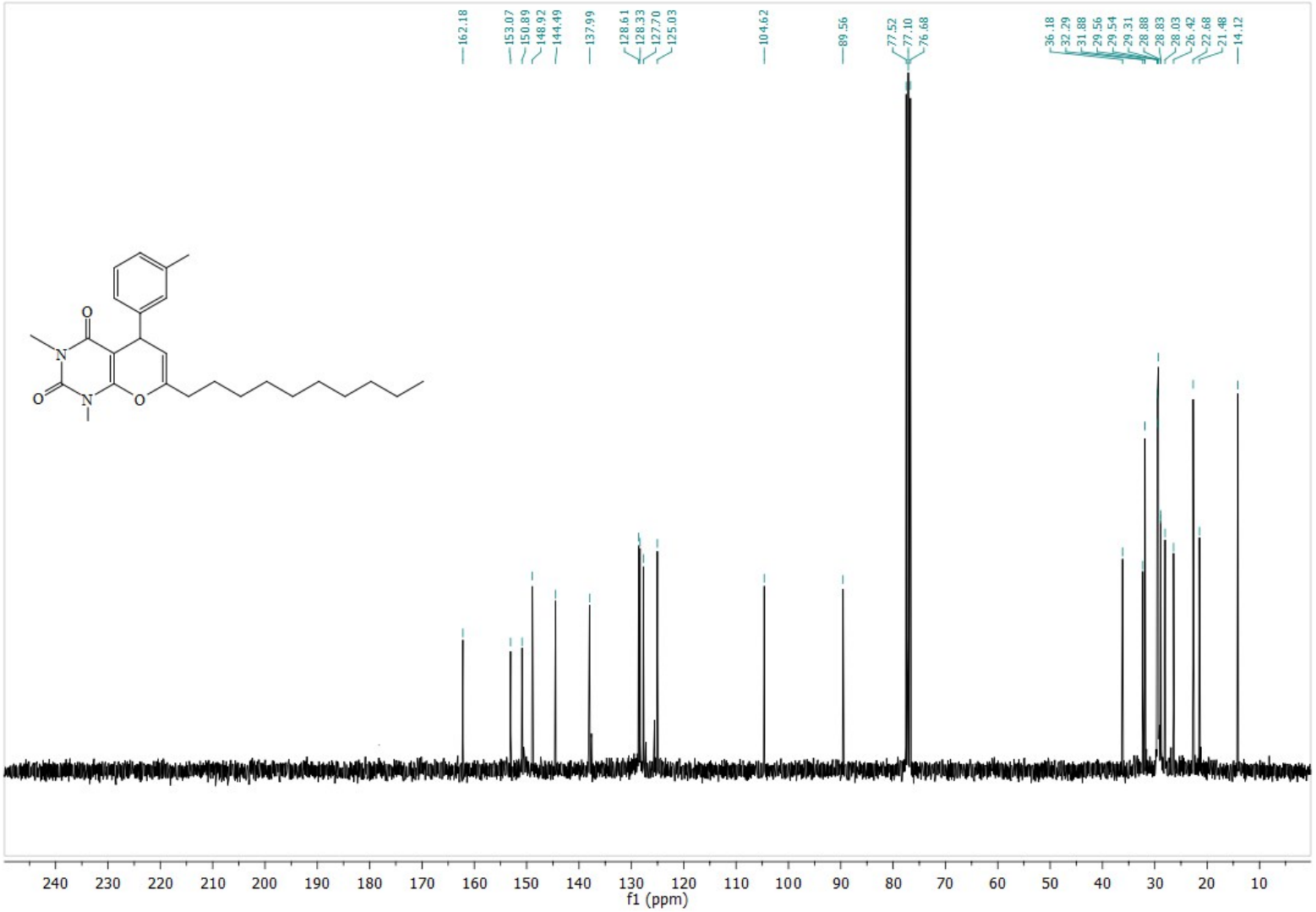
^{1}H NMR Spectrum of compound 4l



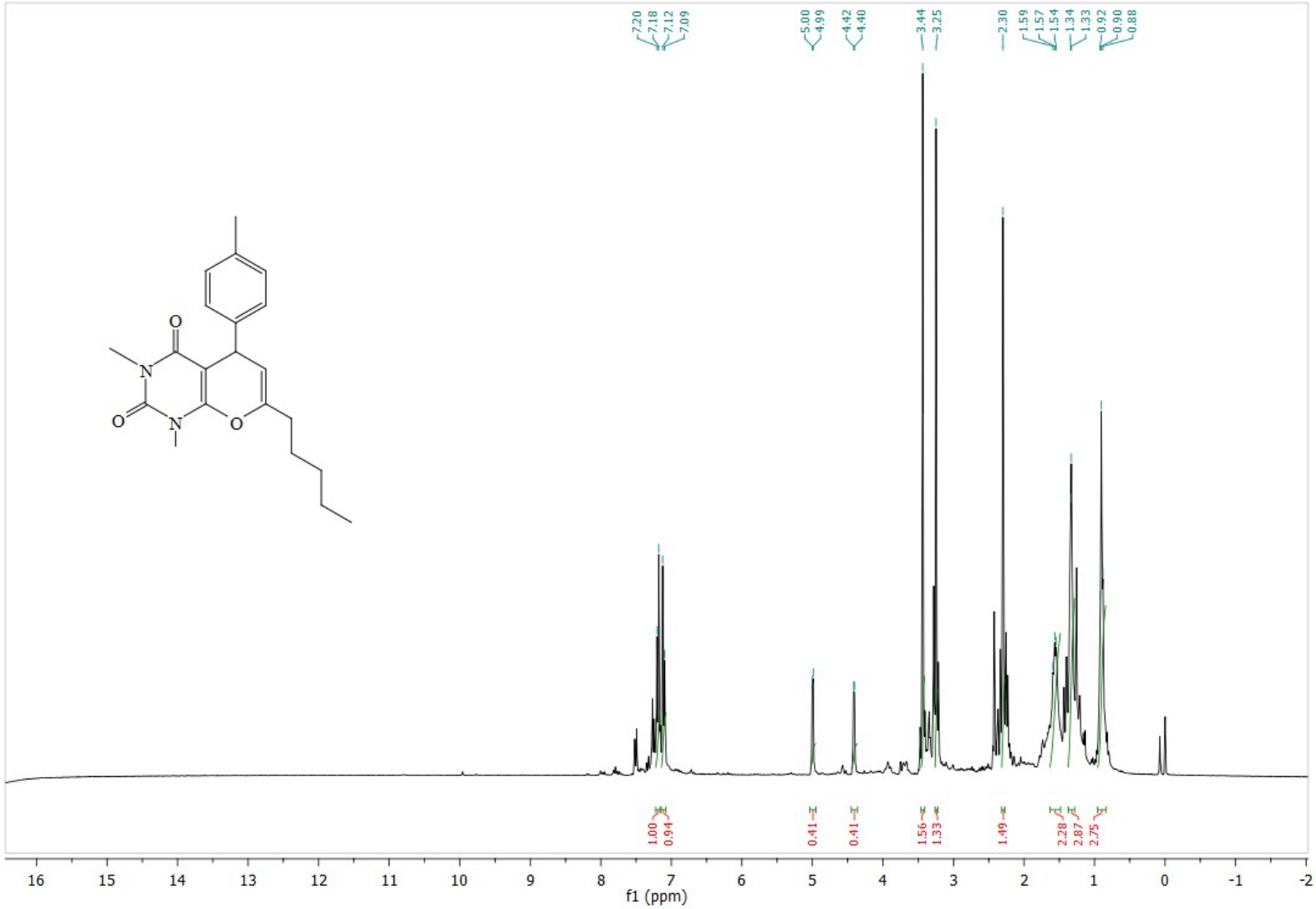
^{13}C NMR Spectrum of compound 4l



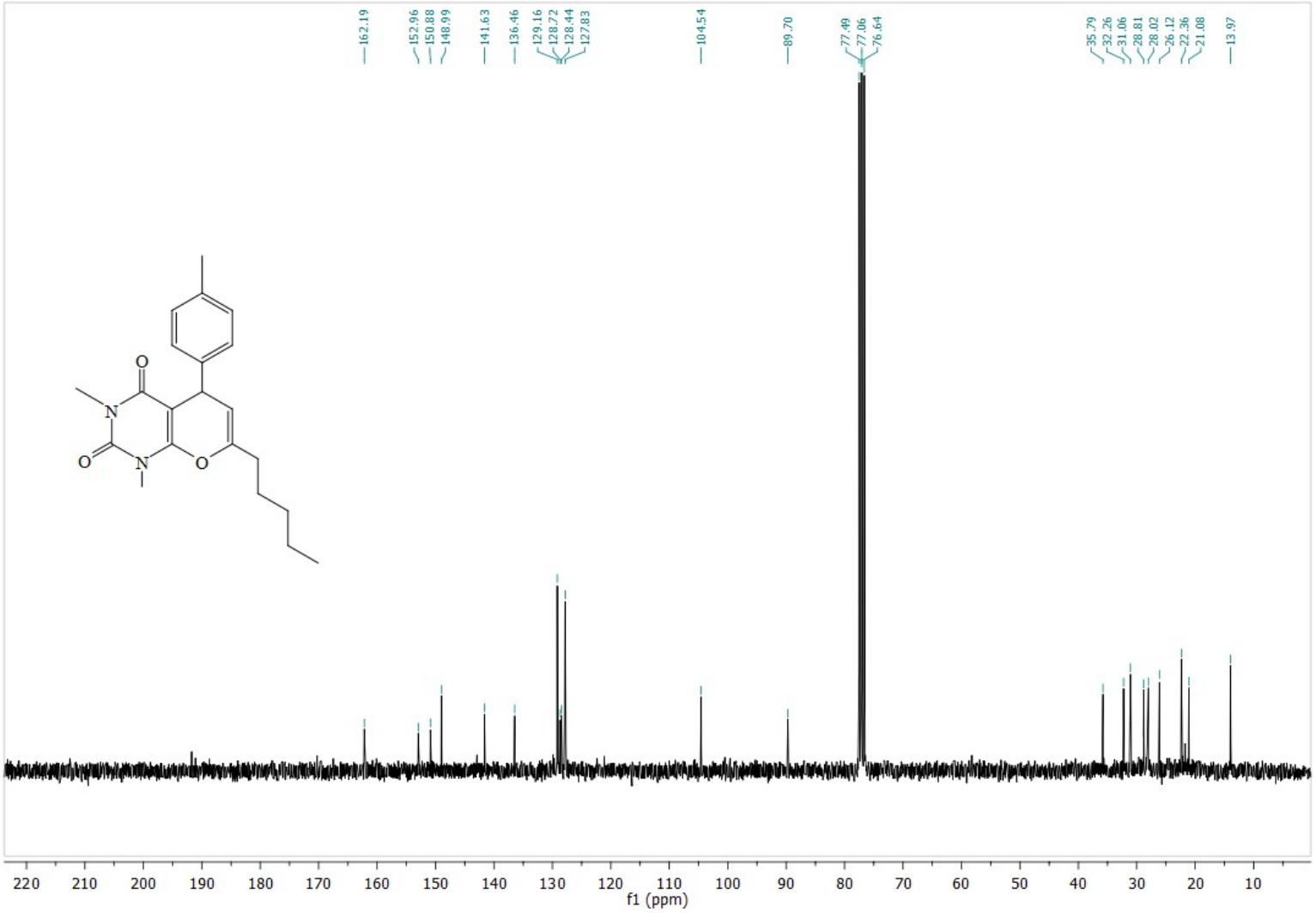
^{1}H NMR Spectrum of compound 4m



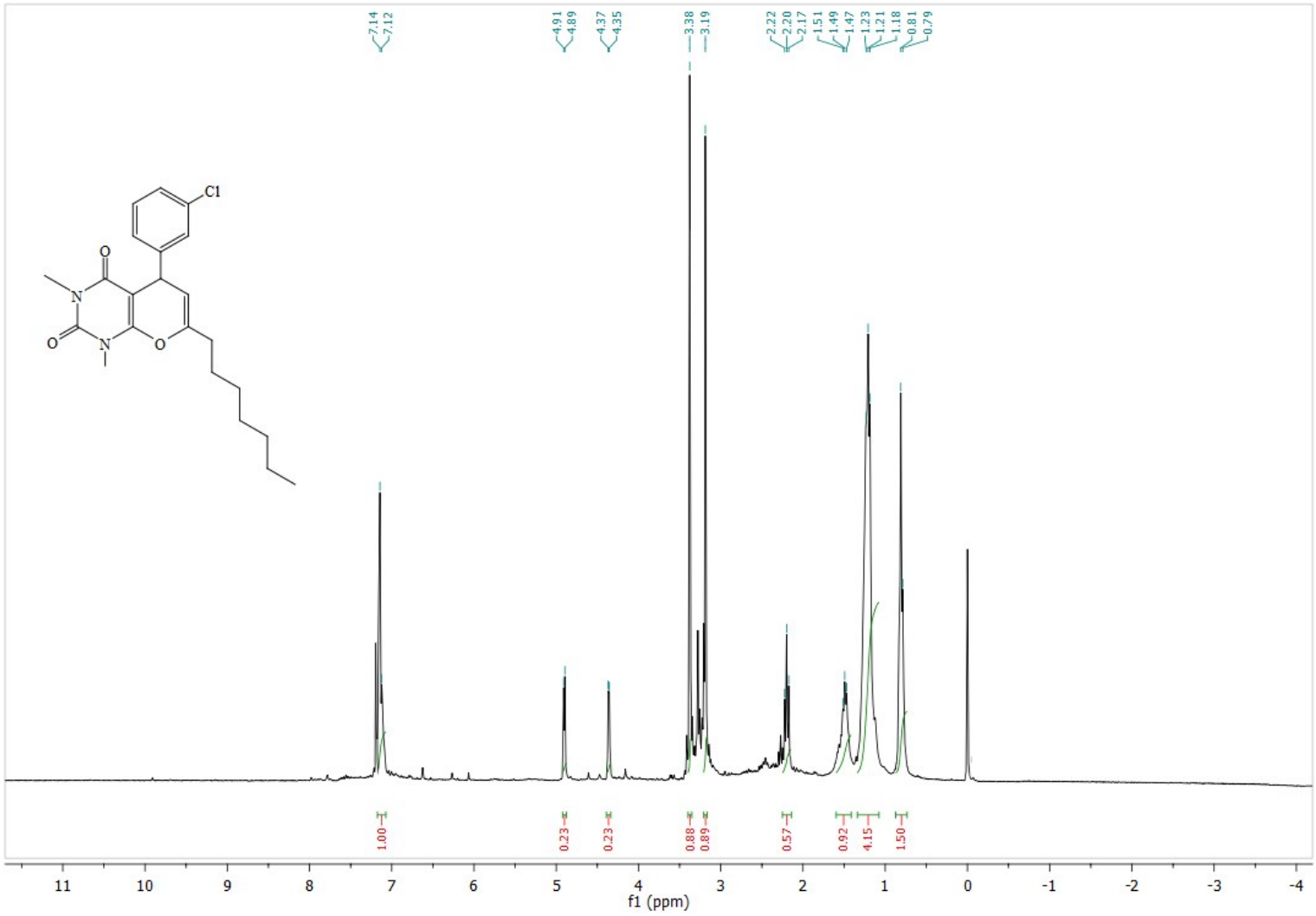
^{13}C NMR Spectrum of compound 4m



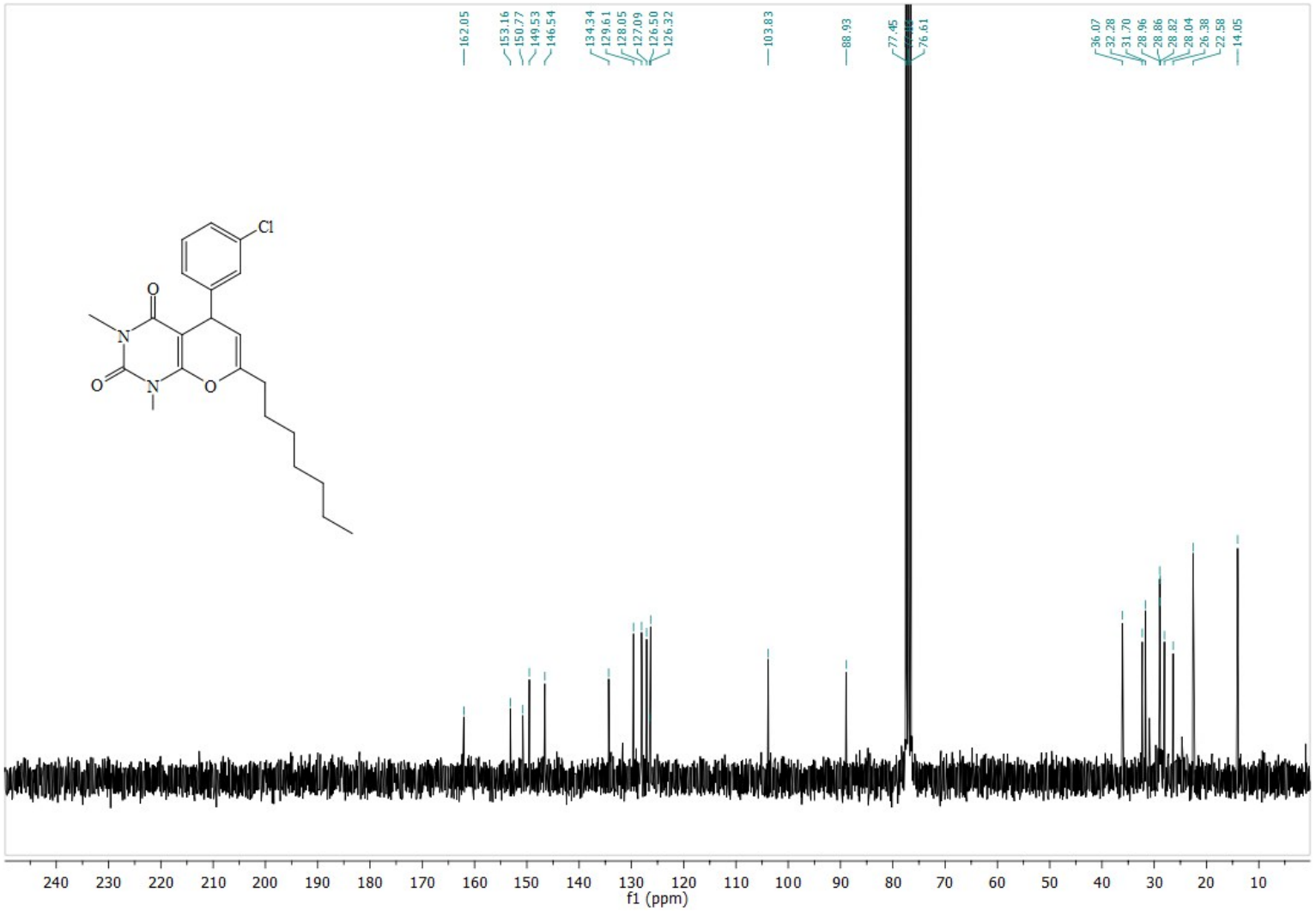
^{1}H NMR Spectrum of compound 4n



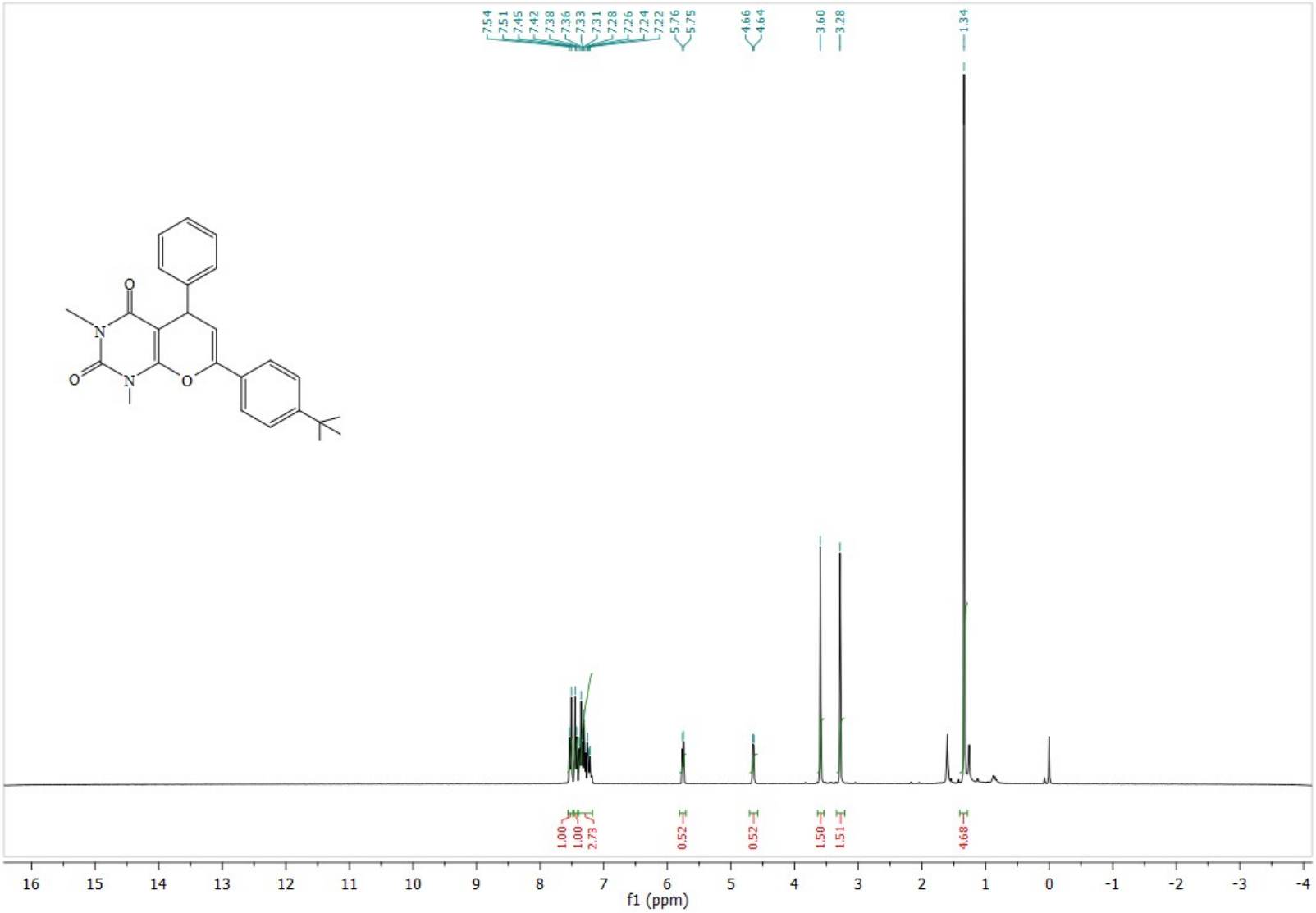
^{13}C NMR Spectrum of compound 4n



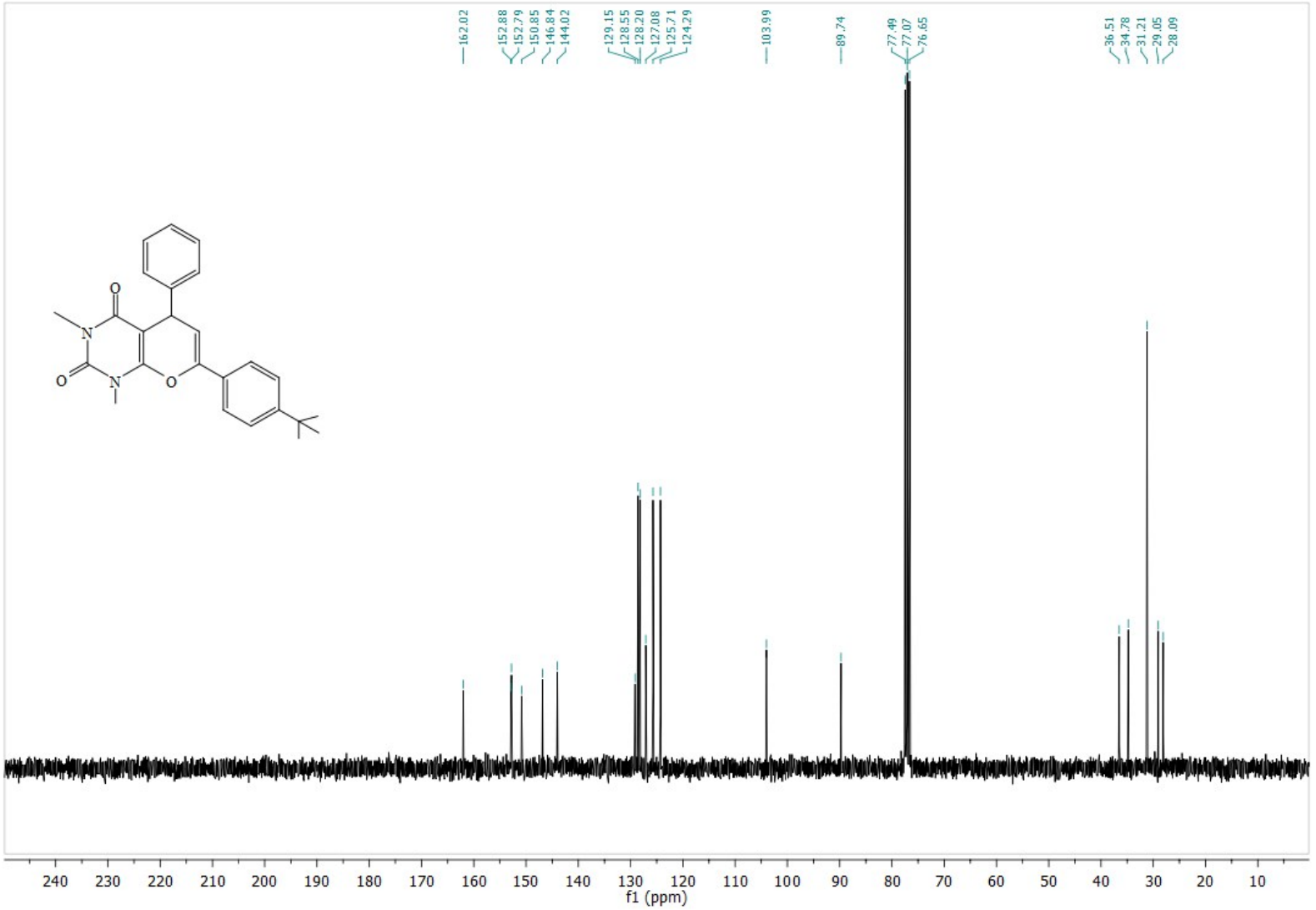
^{1}H NMR Spectrum of compound 4o



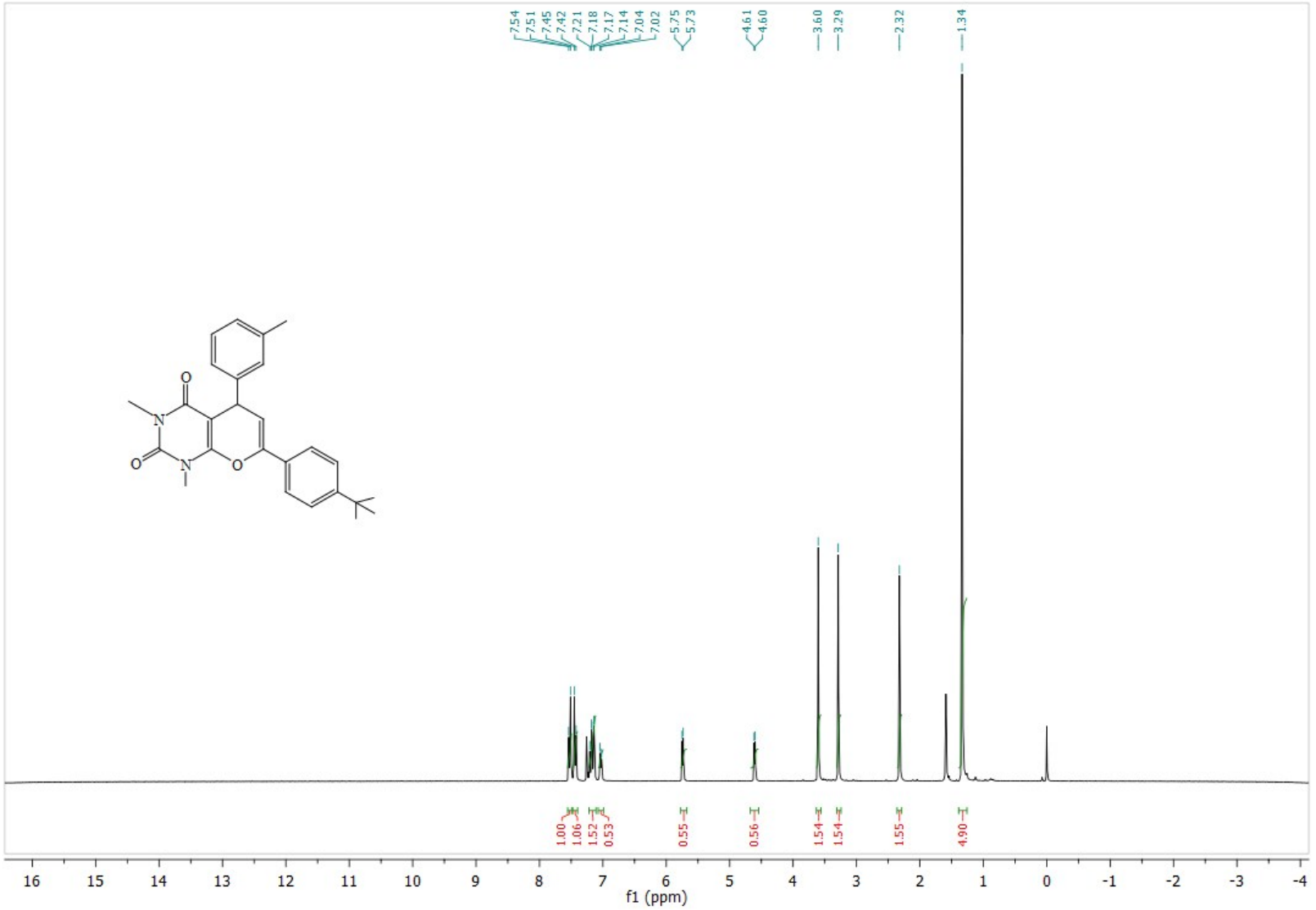
^{13}C NMR Spectrum of compound 4o



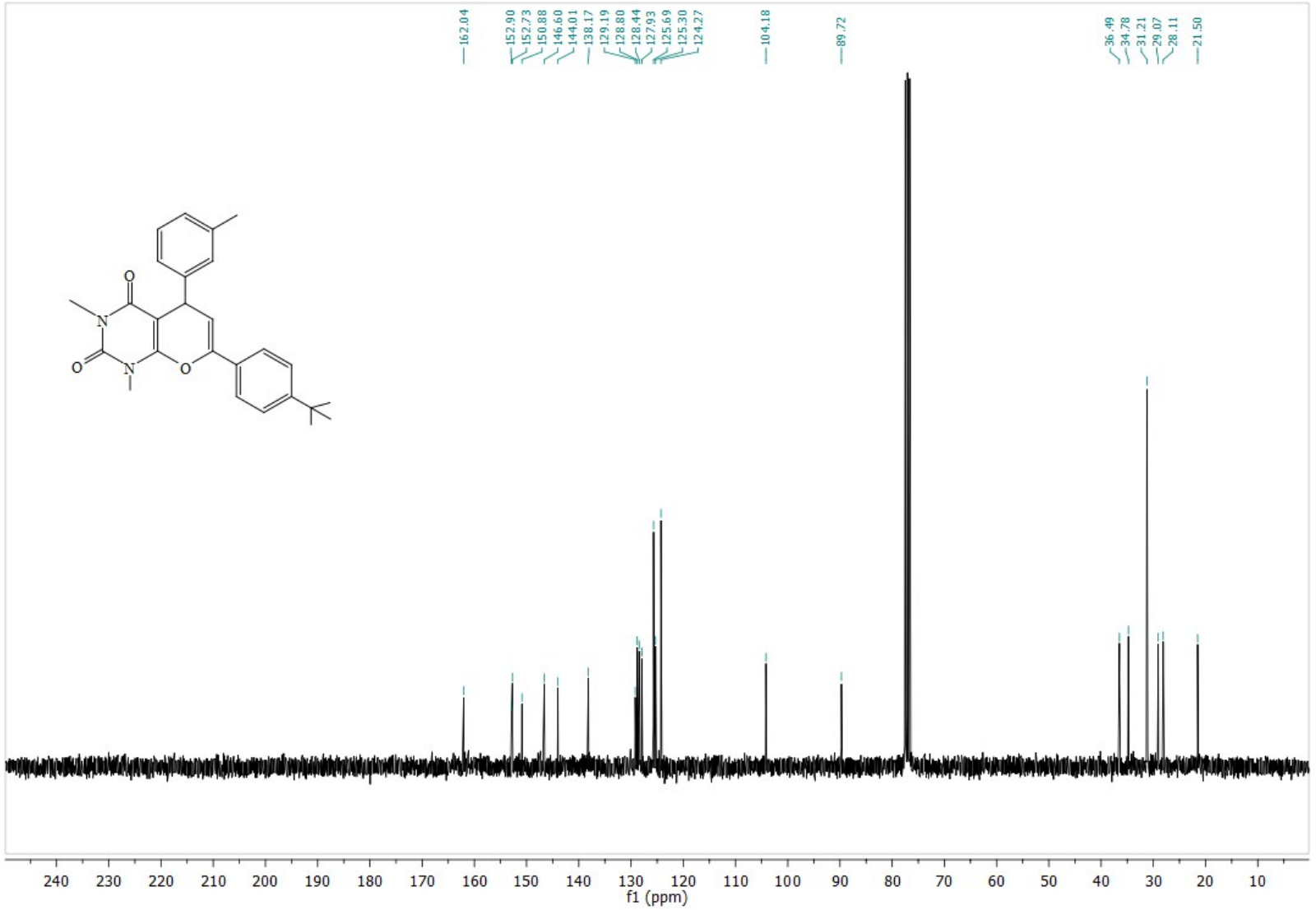
[1]H NMR Spectrum of compound 4p



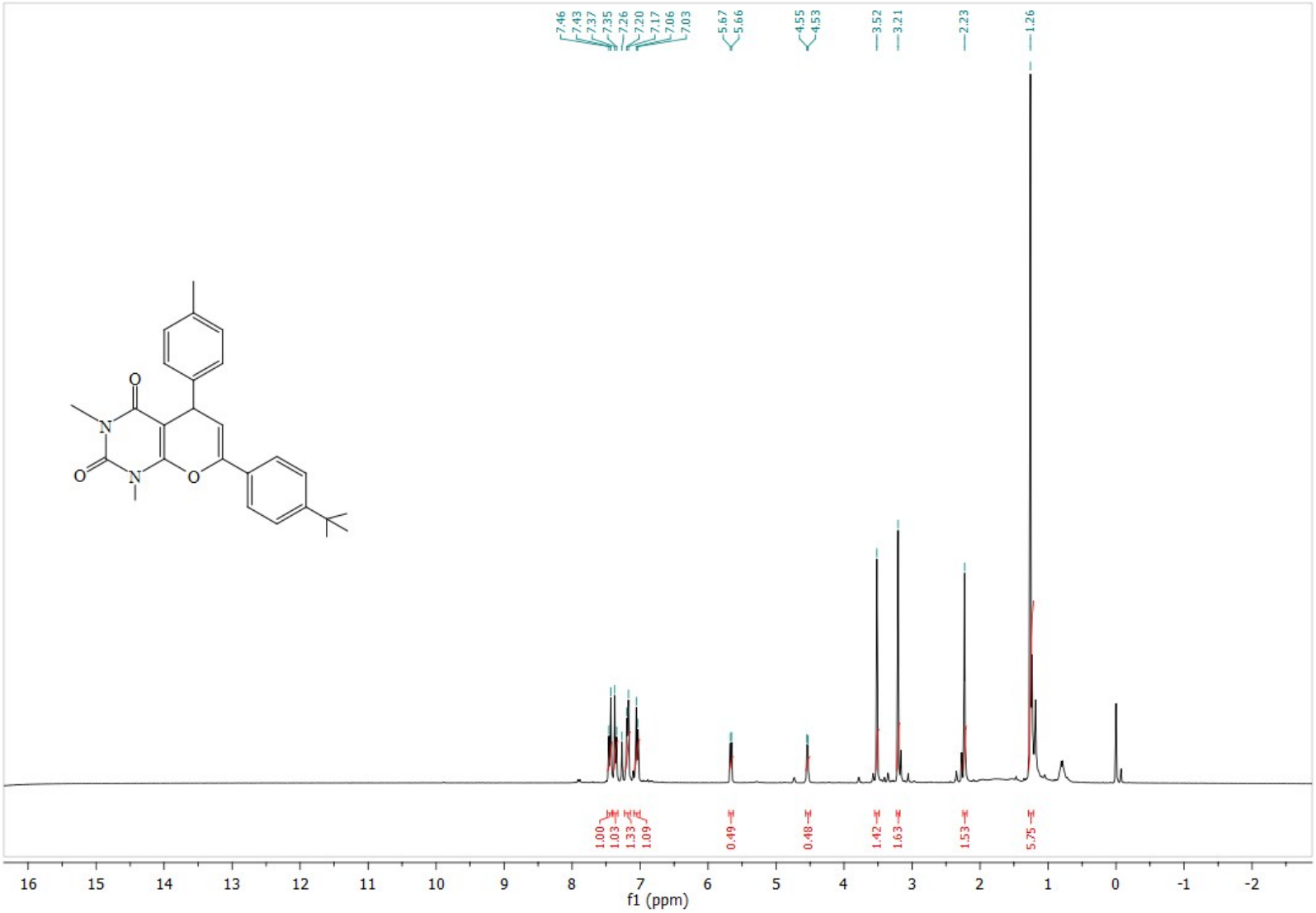
^{13}C NMR Spectrum of compound 4p



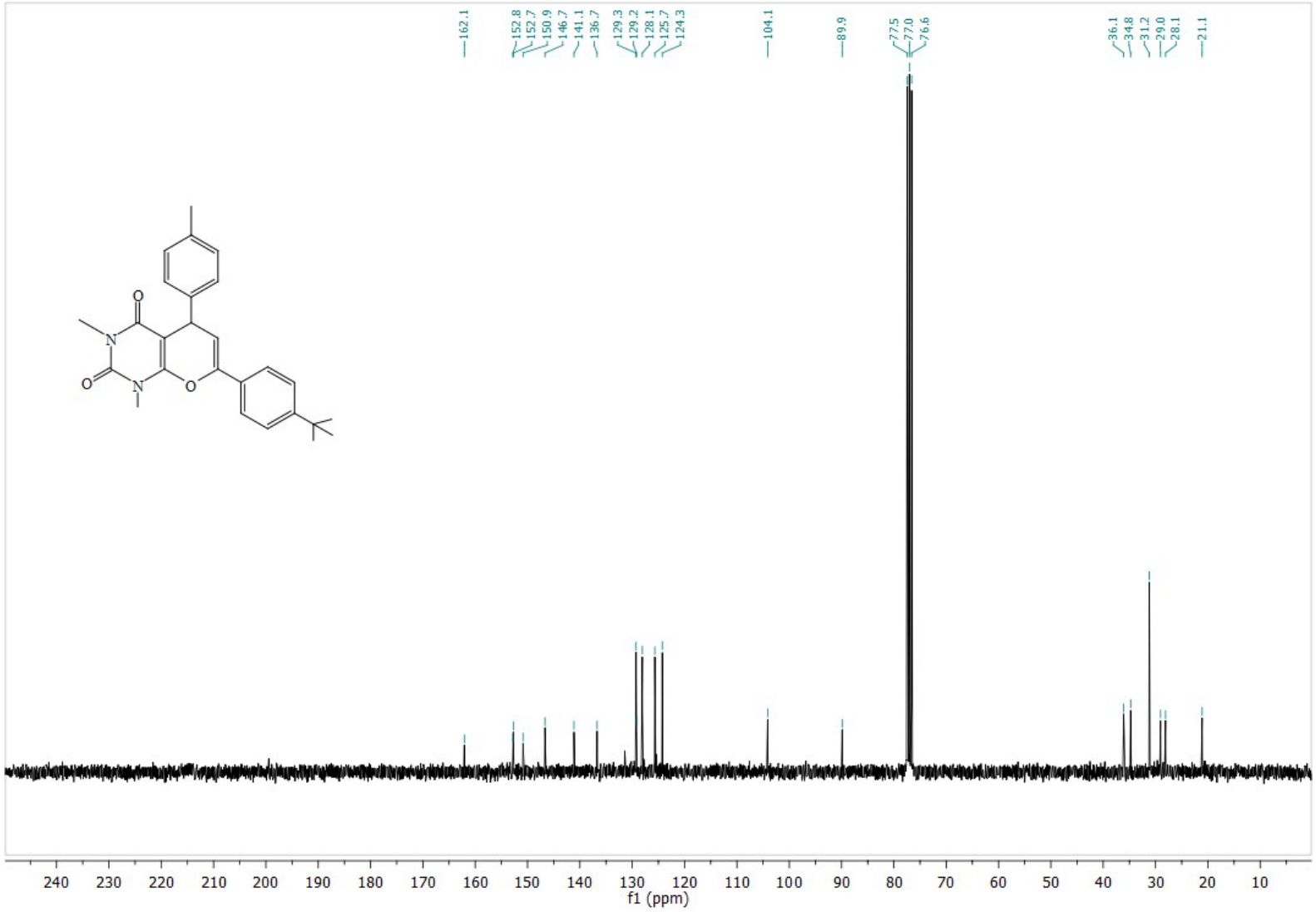
^{1}H NMR Spectrum of compound 4q



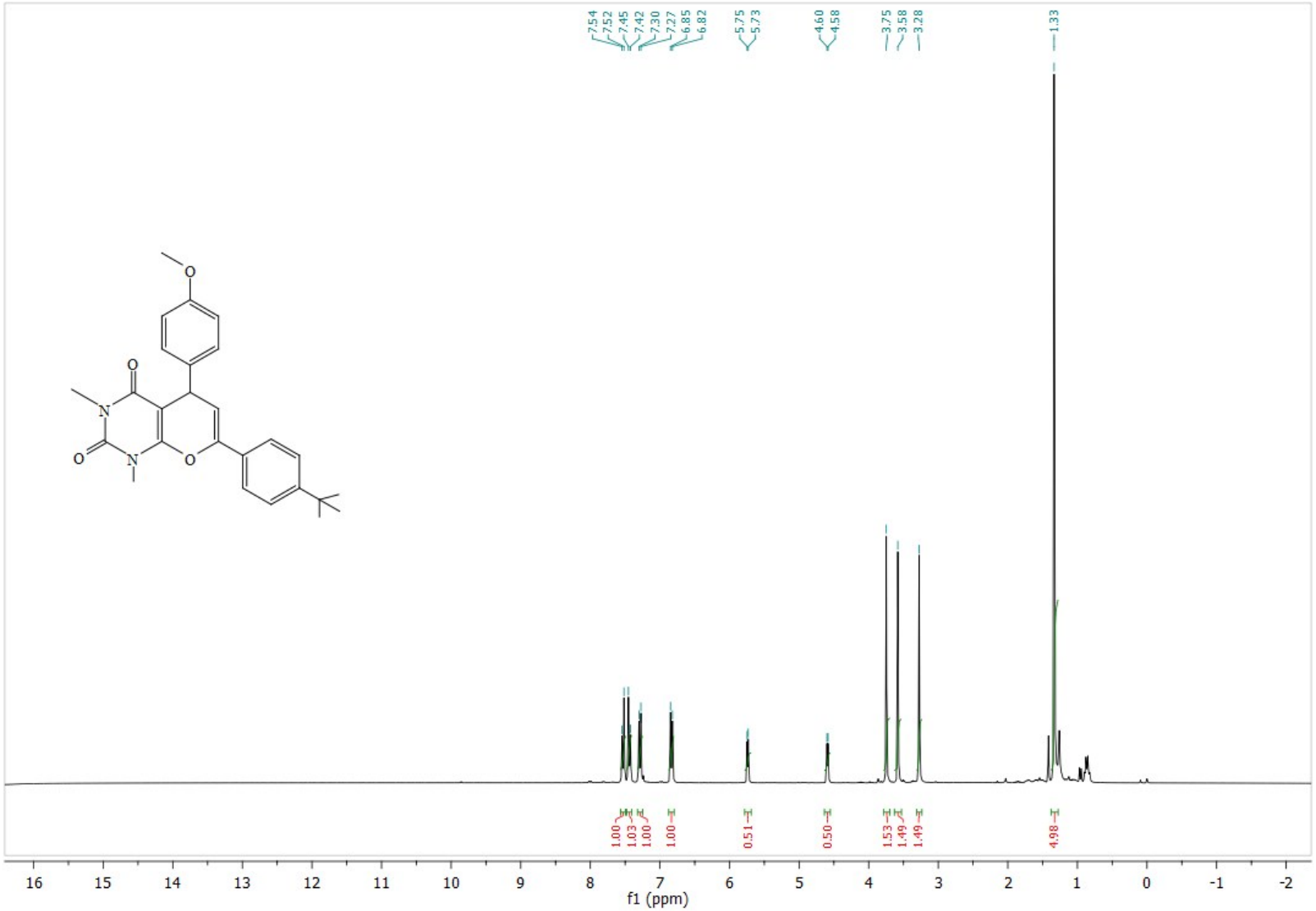
^{13}C NMR Spectrum of compound 4q



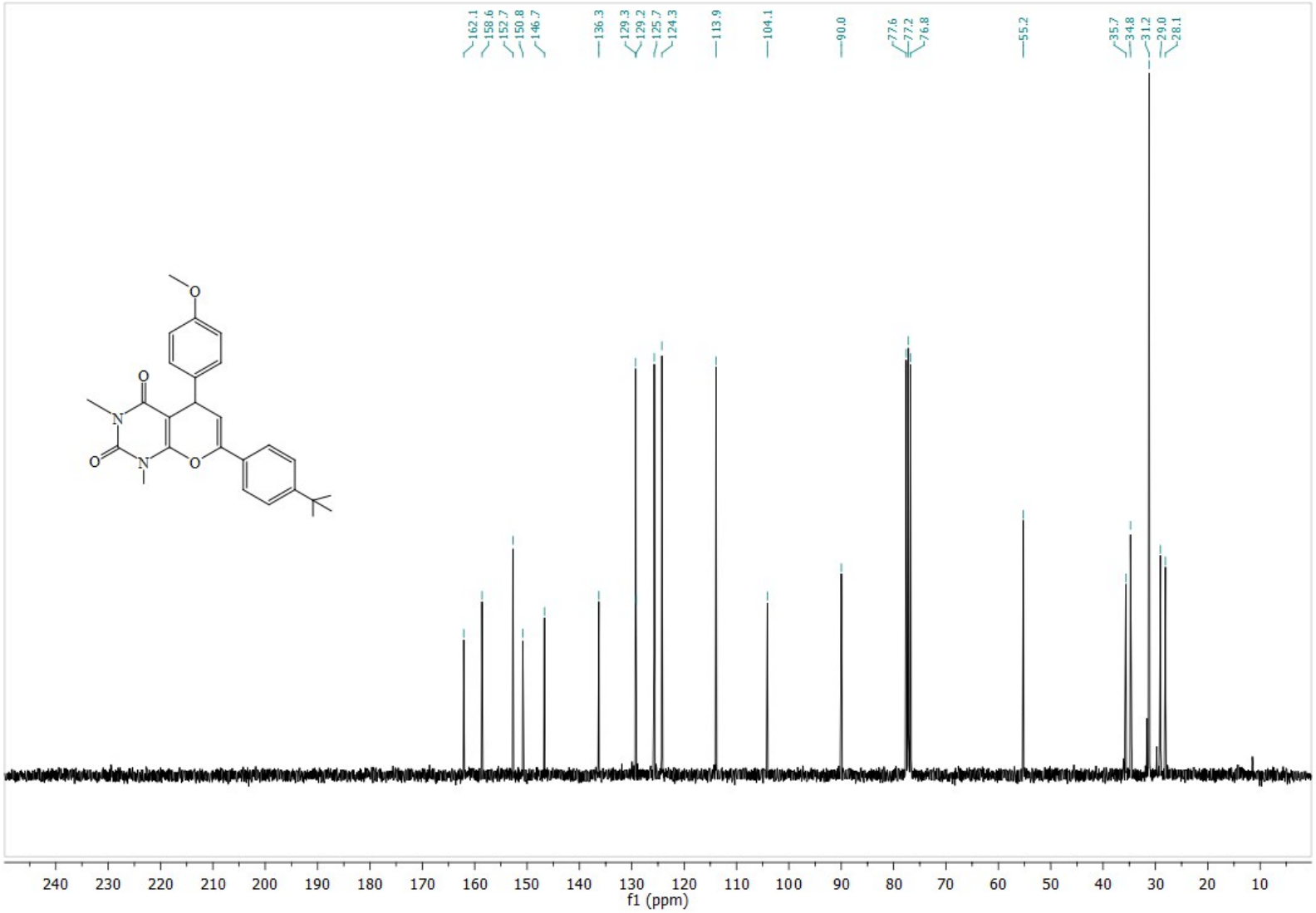
[1]H NMR Spectrum of compound 4r



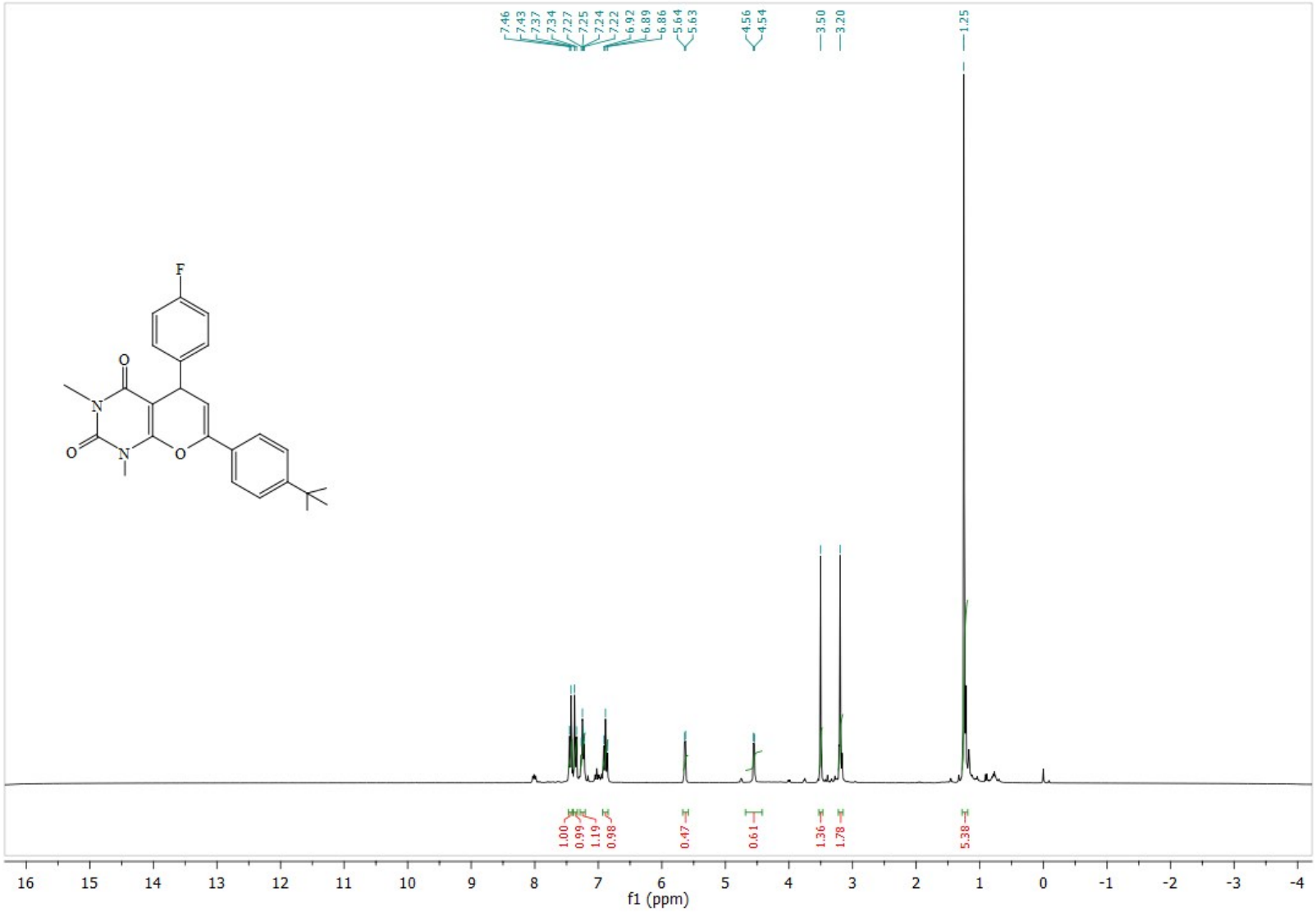
^{13}C NMR Spectrum of compound 4r



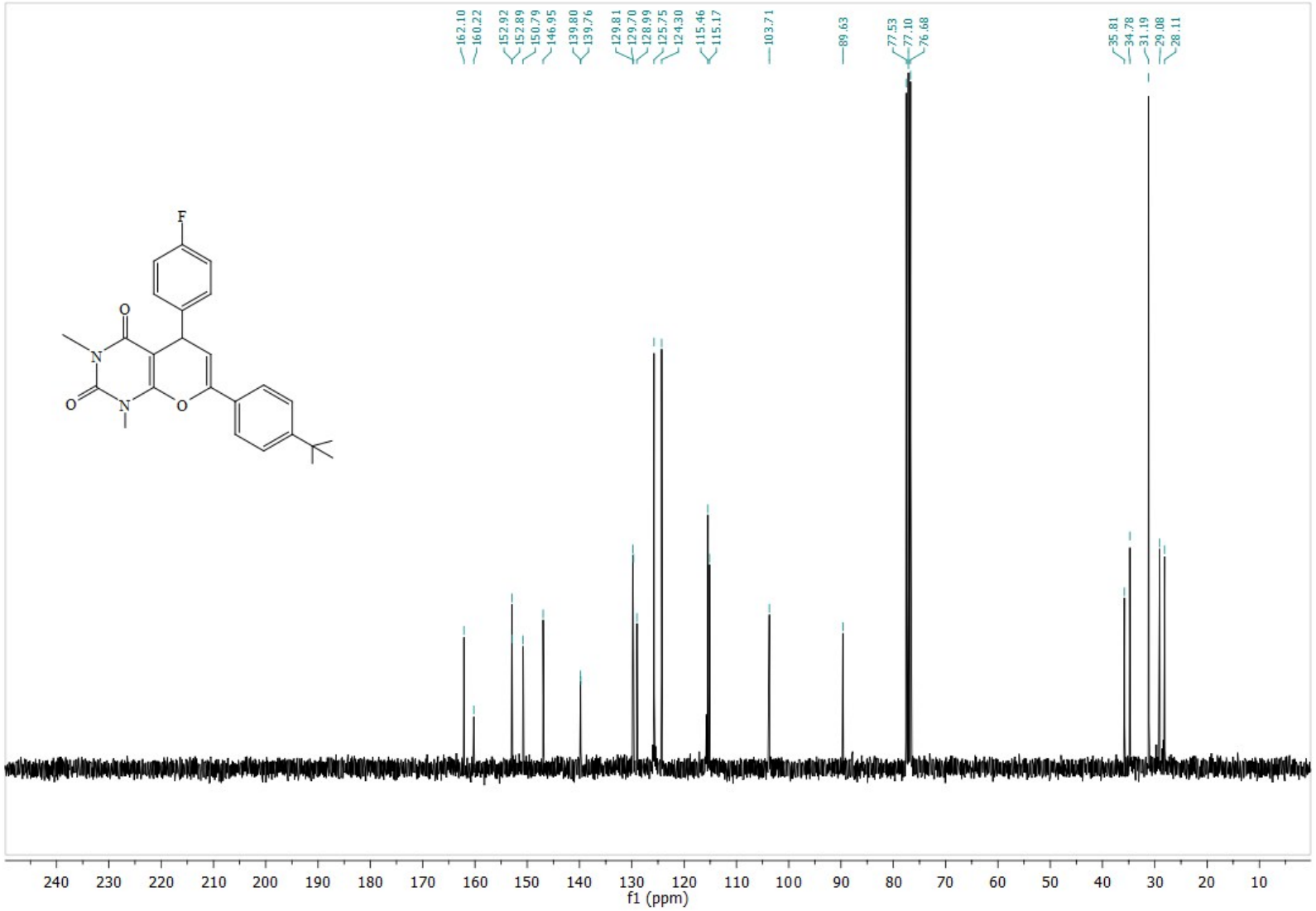
[1]H NMR Spectrum of compound 4s



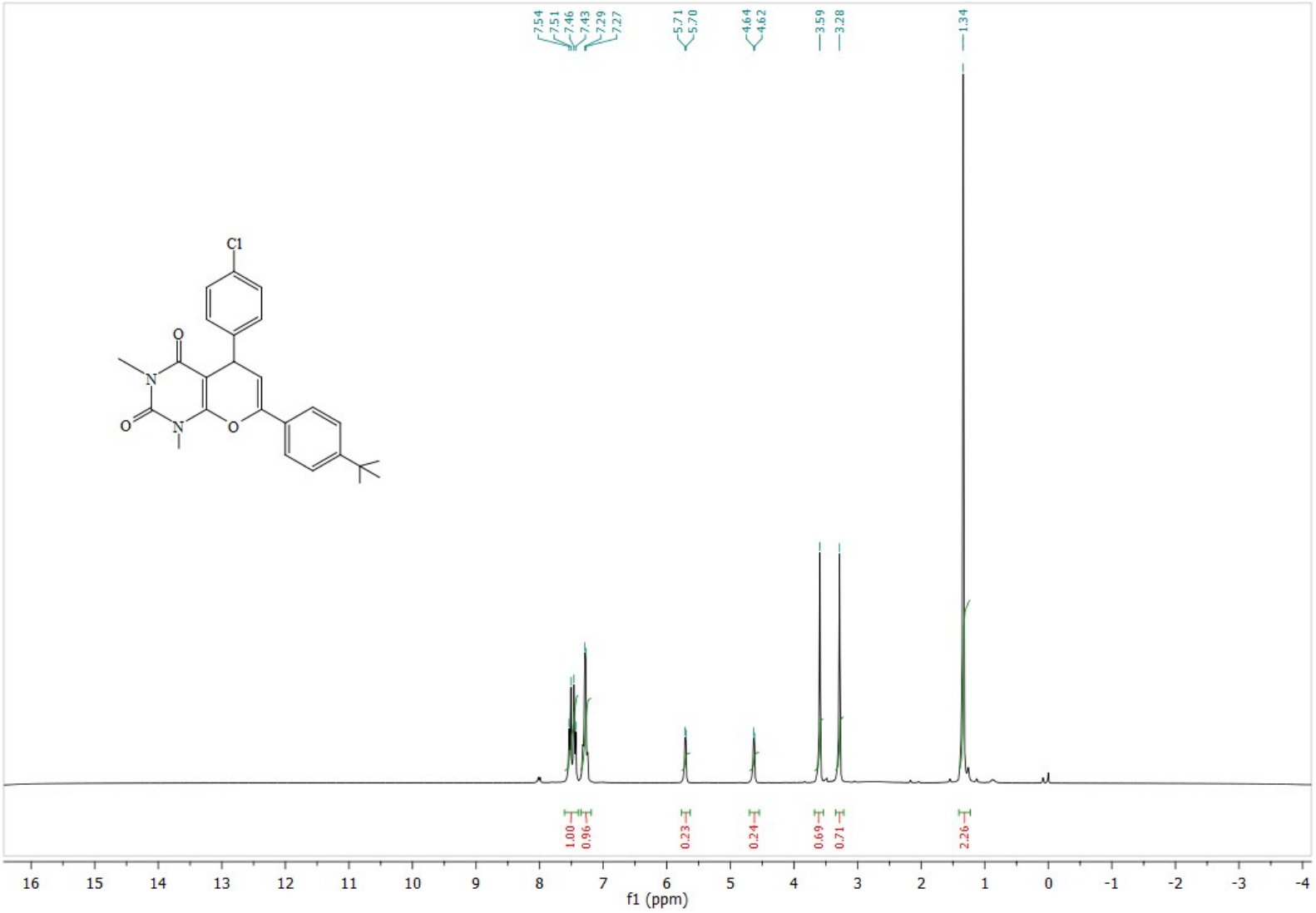
^{13}C NMR Spectrum of compound 4s



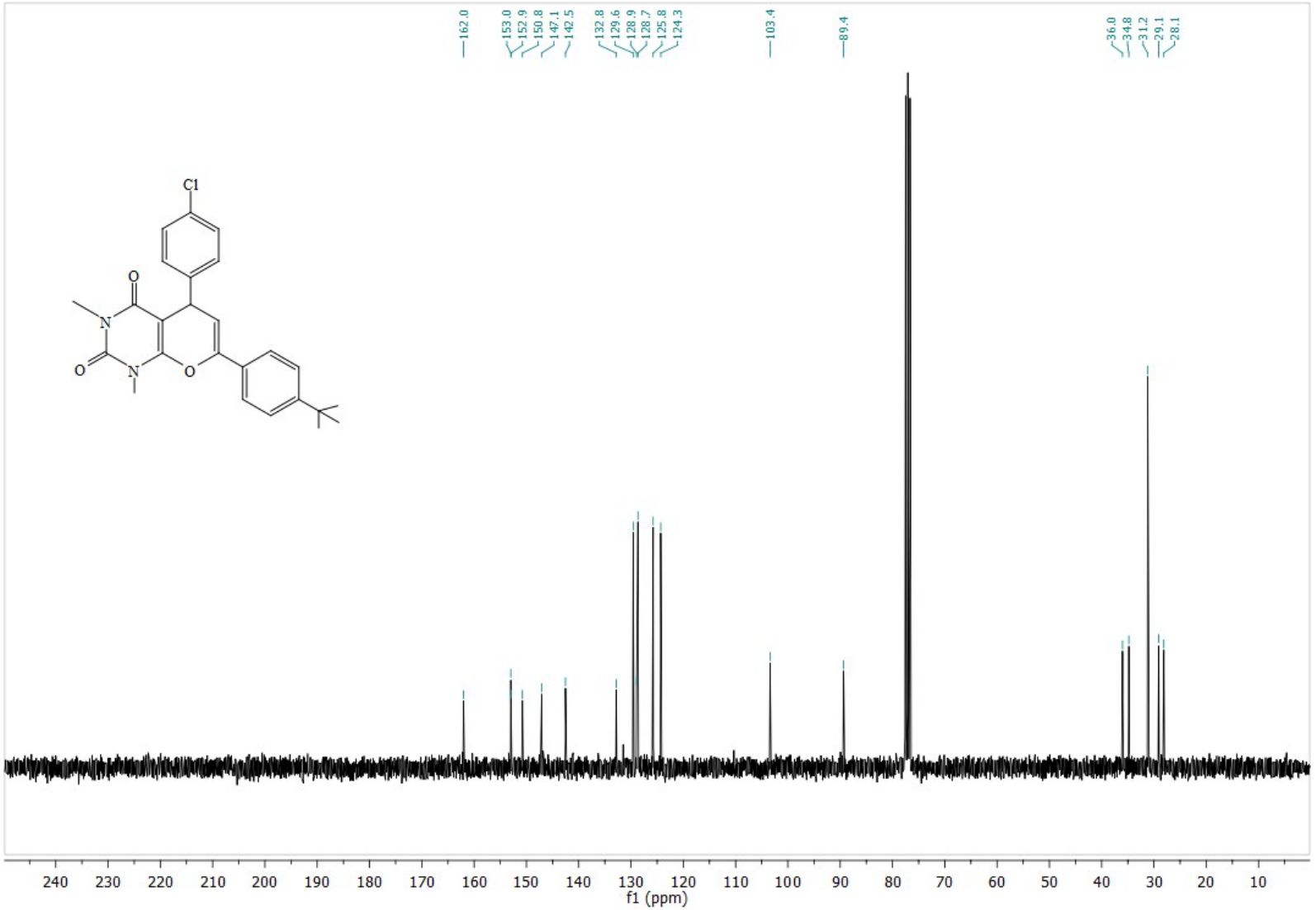
^{1}H NMR Spectrum of compound 4t



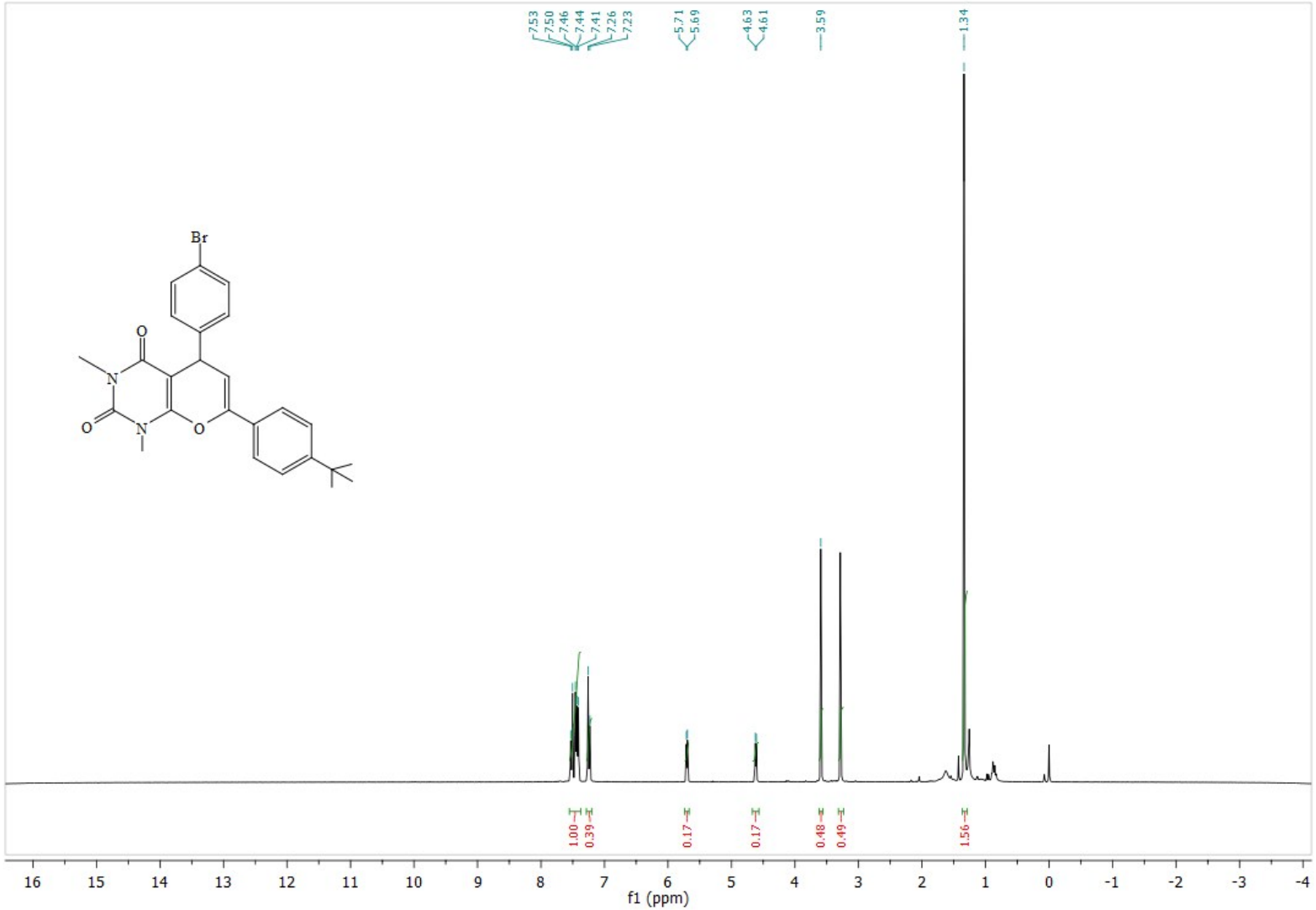
^{13}C NMR Spectrum of compound 4t



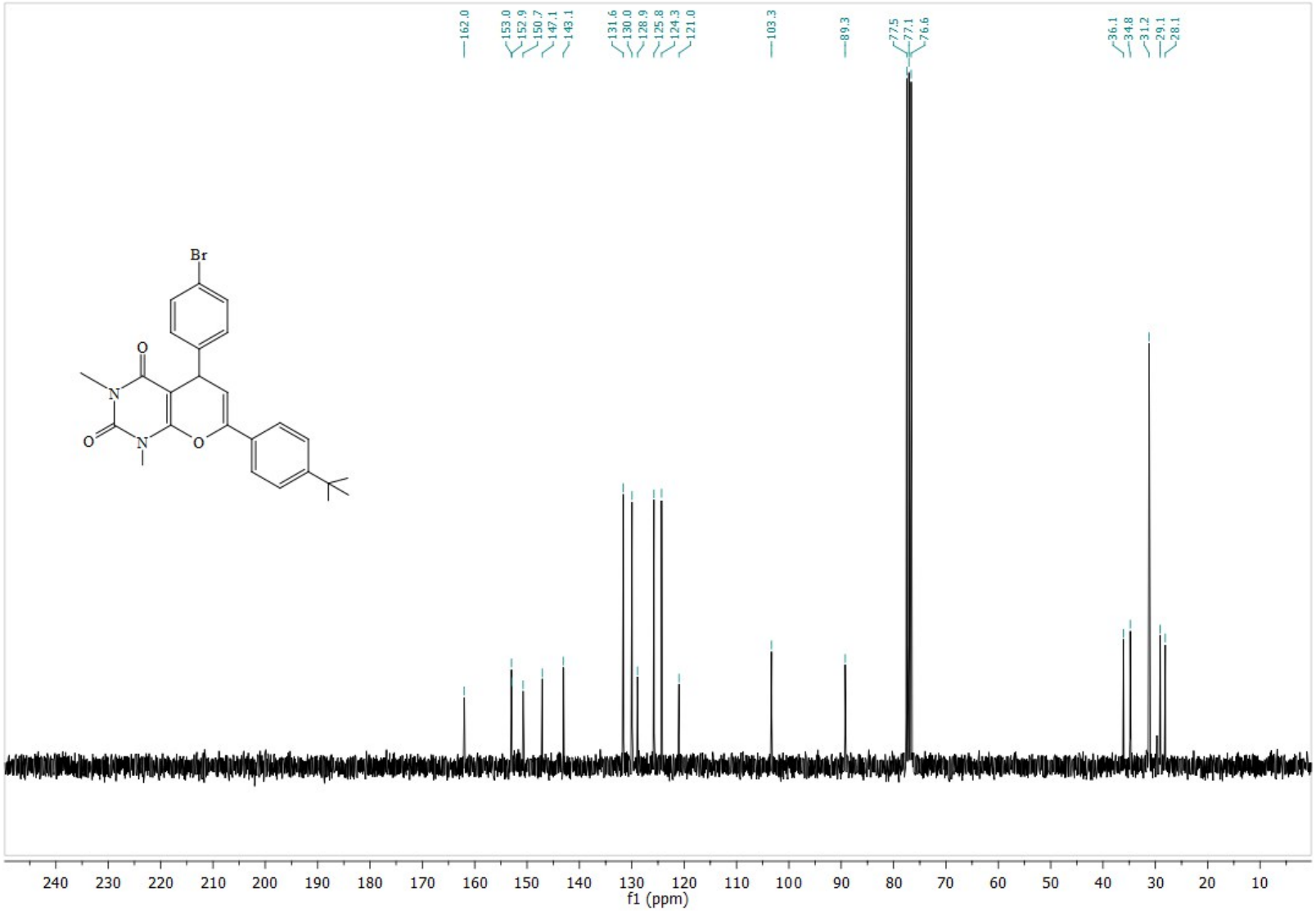
^{1}H NMR Spectrum of compound 4u



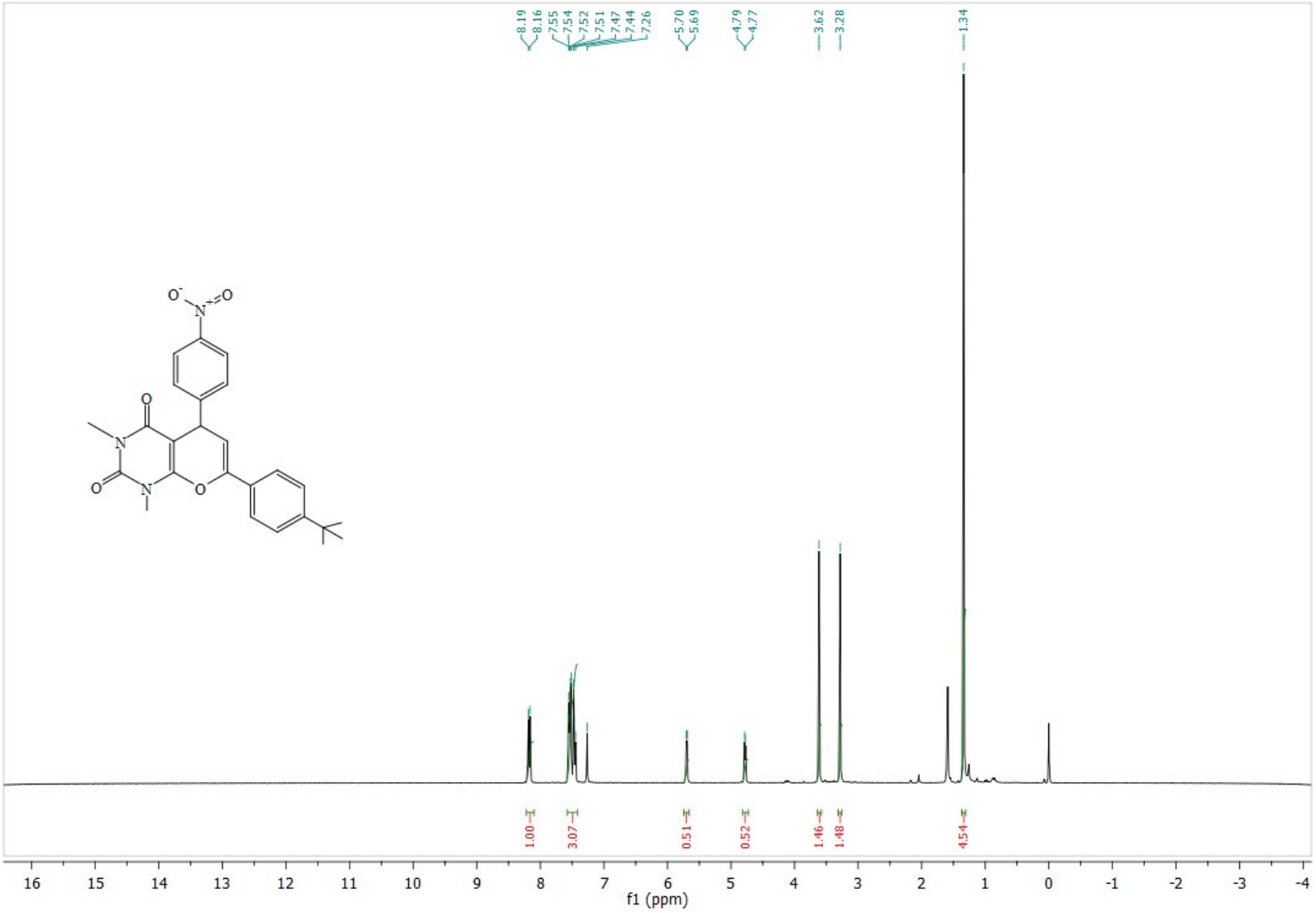
^{13}C NMR Spectrum of compound 4u



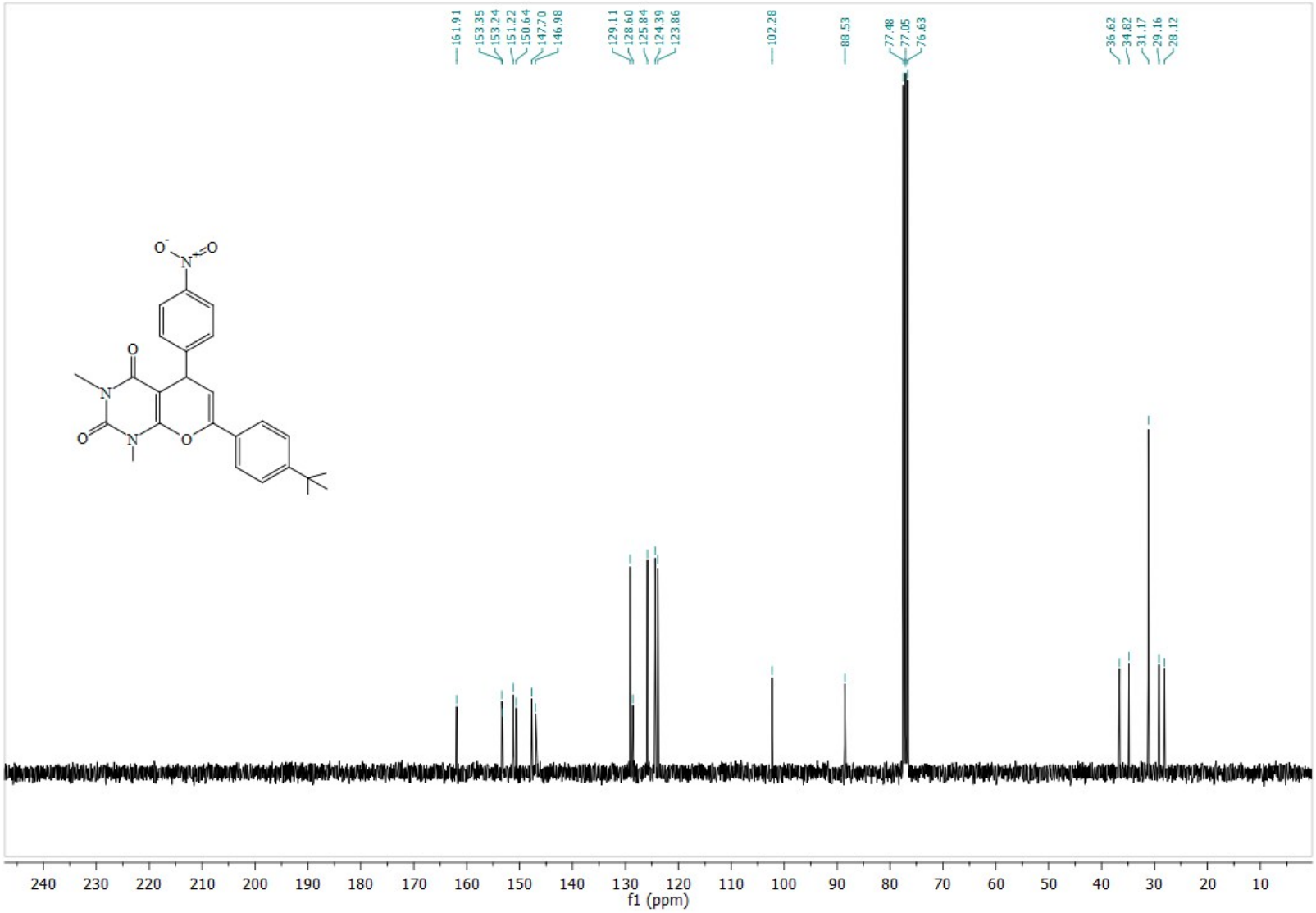
^{1}H NMR Spectrum of compound 4v



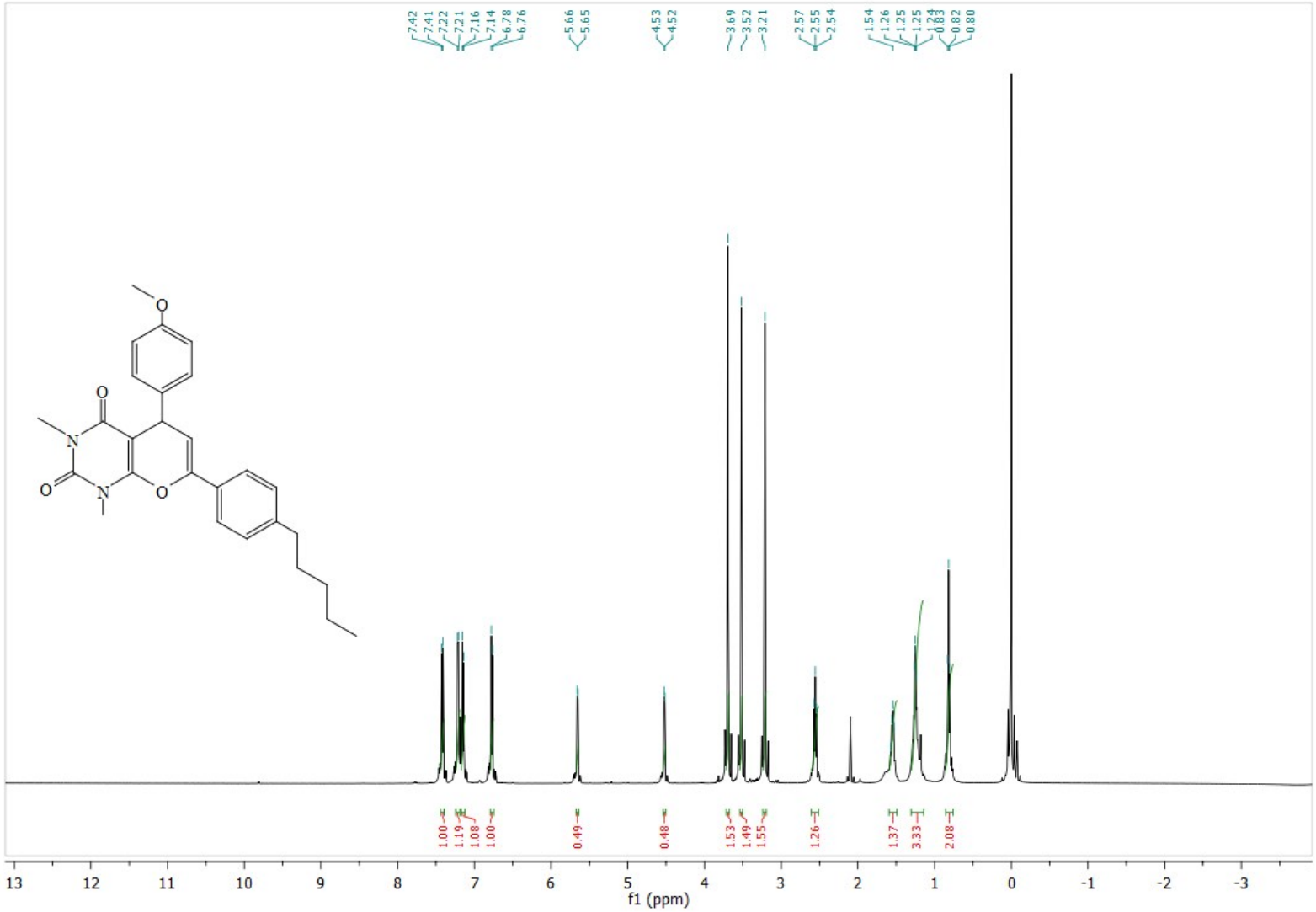
^{13}C NMR Spectrum of compound 4v



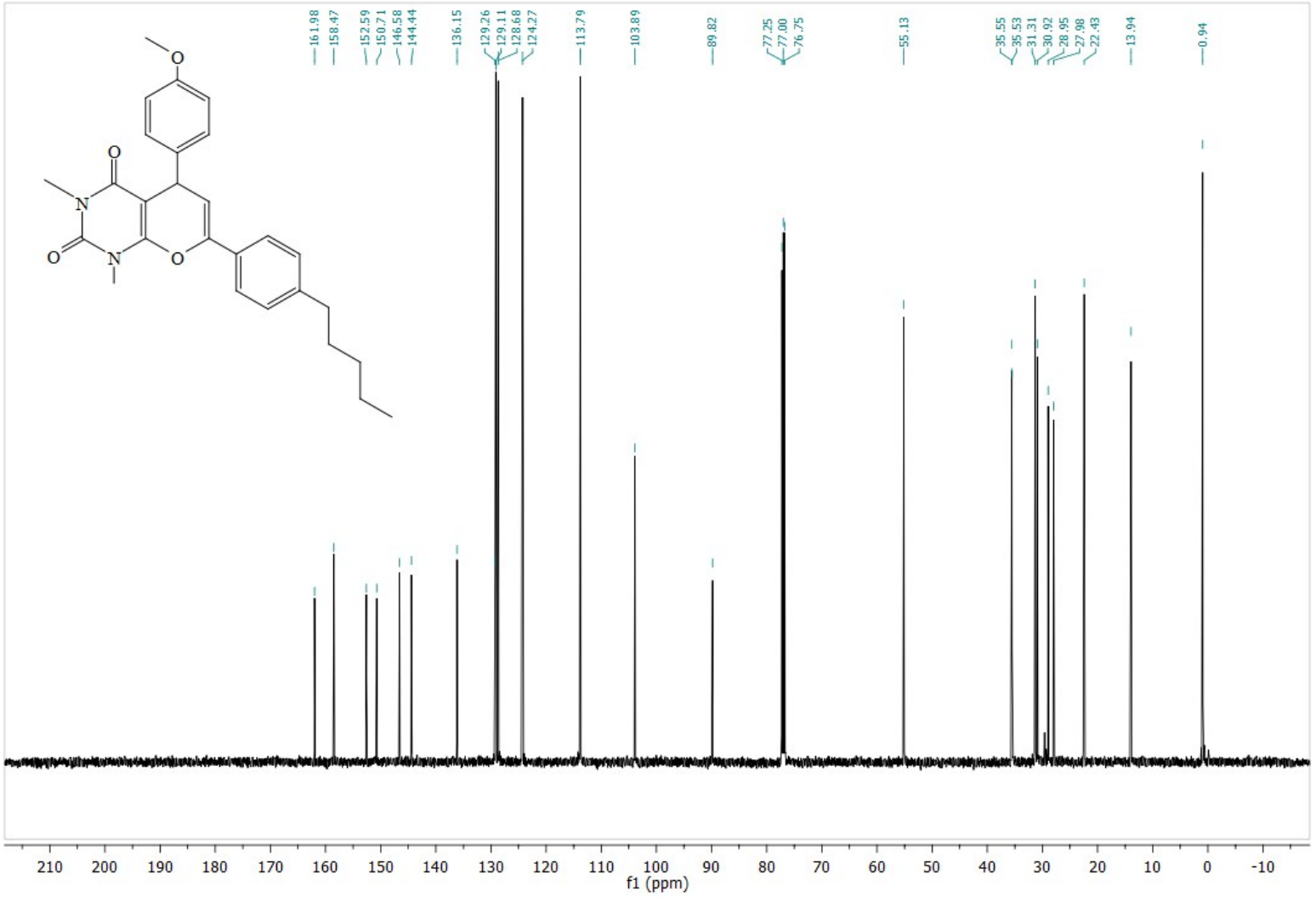
^{1}H NMR Spectrum of compound 4w



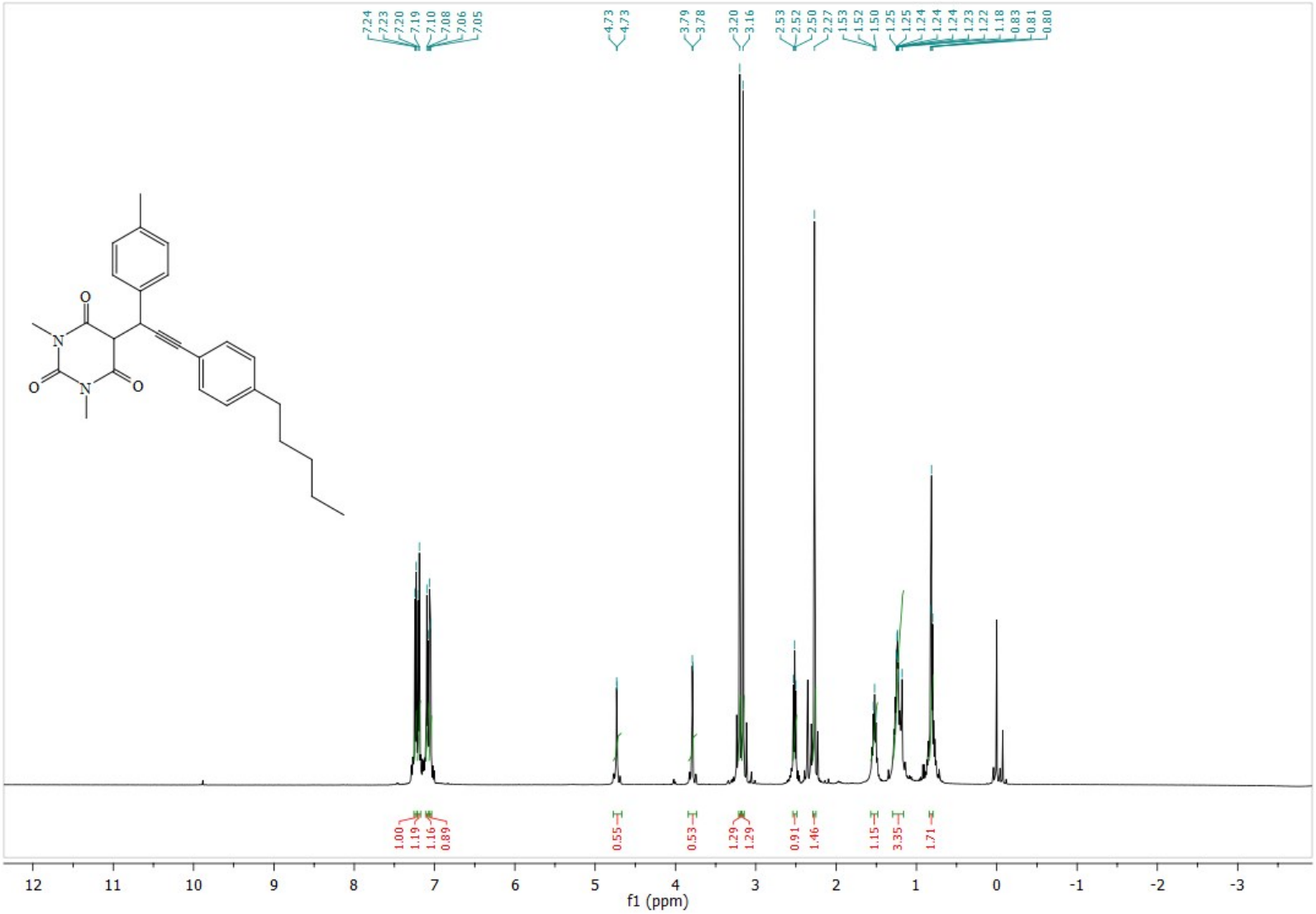
^{13}C NMR Spectrum of compound 4w



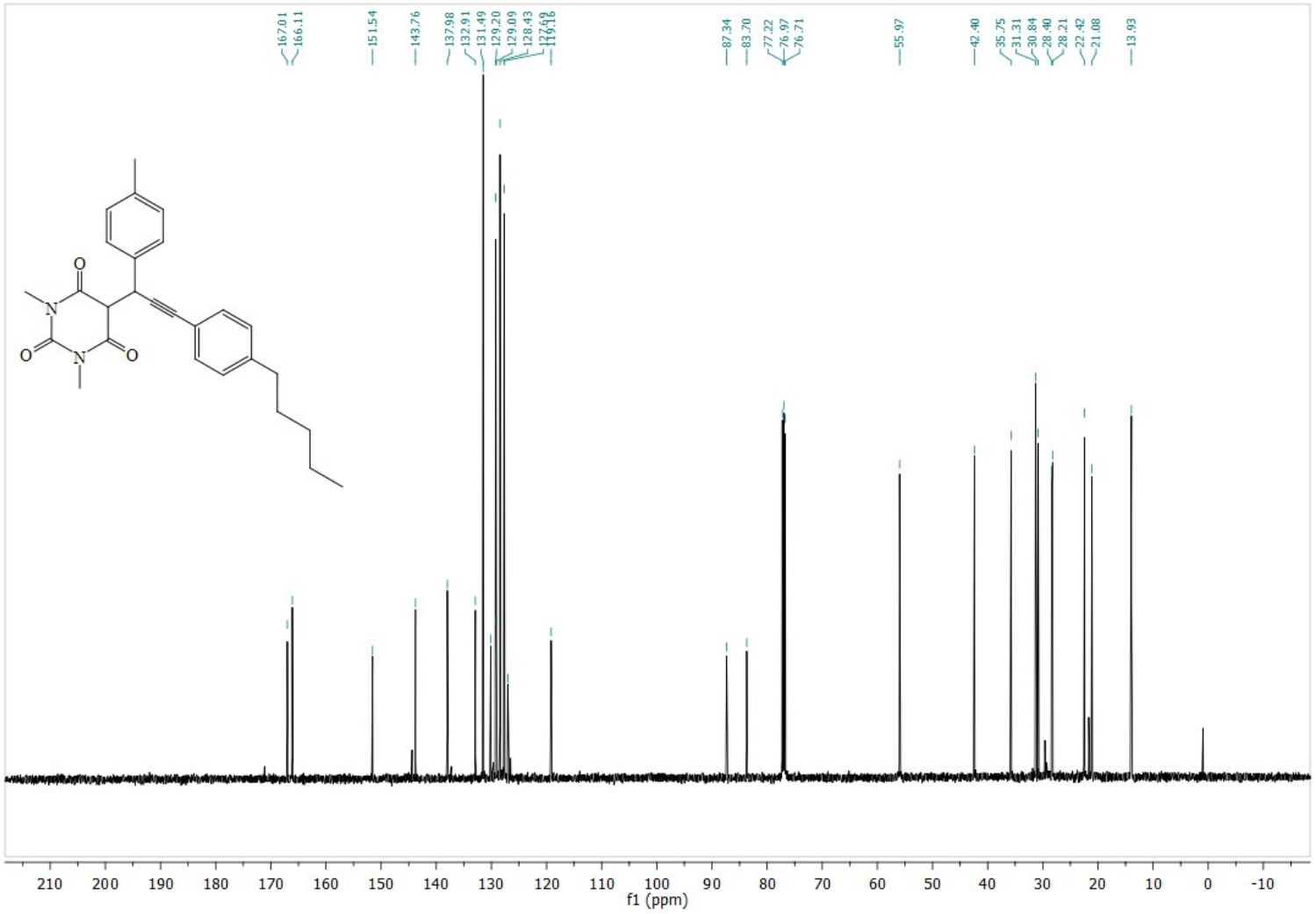
^{1}H NMR Spectrum of compound 4x



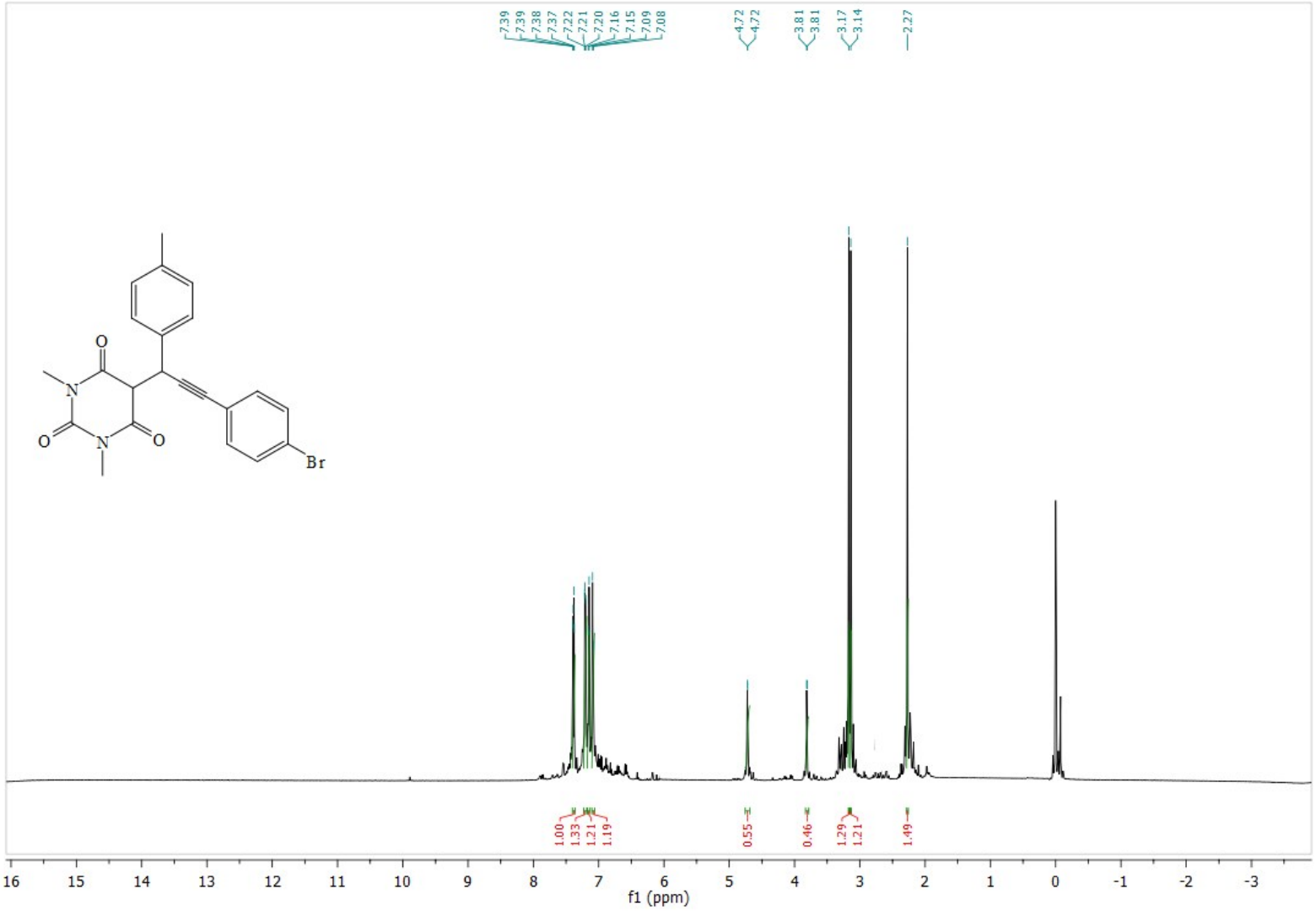
^{13}C NMR Spectrum of compound 4x



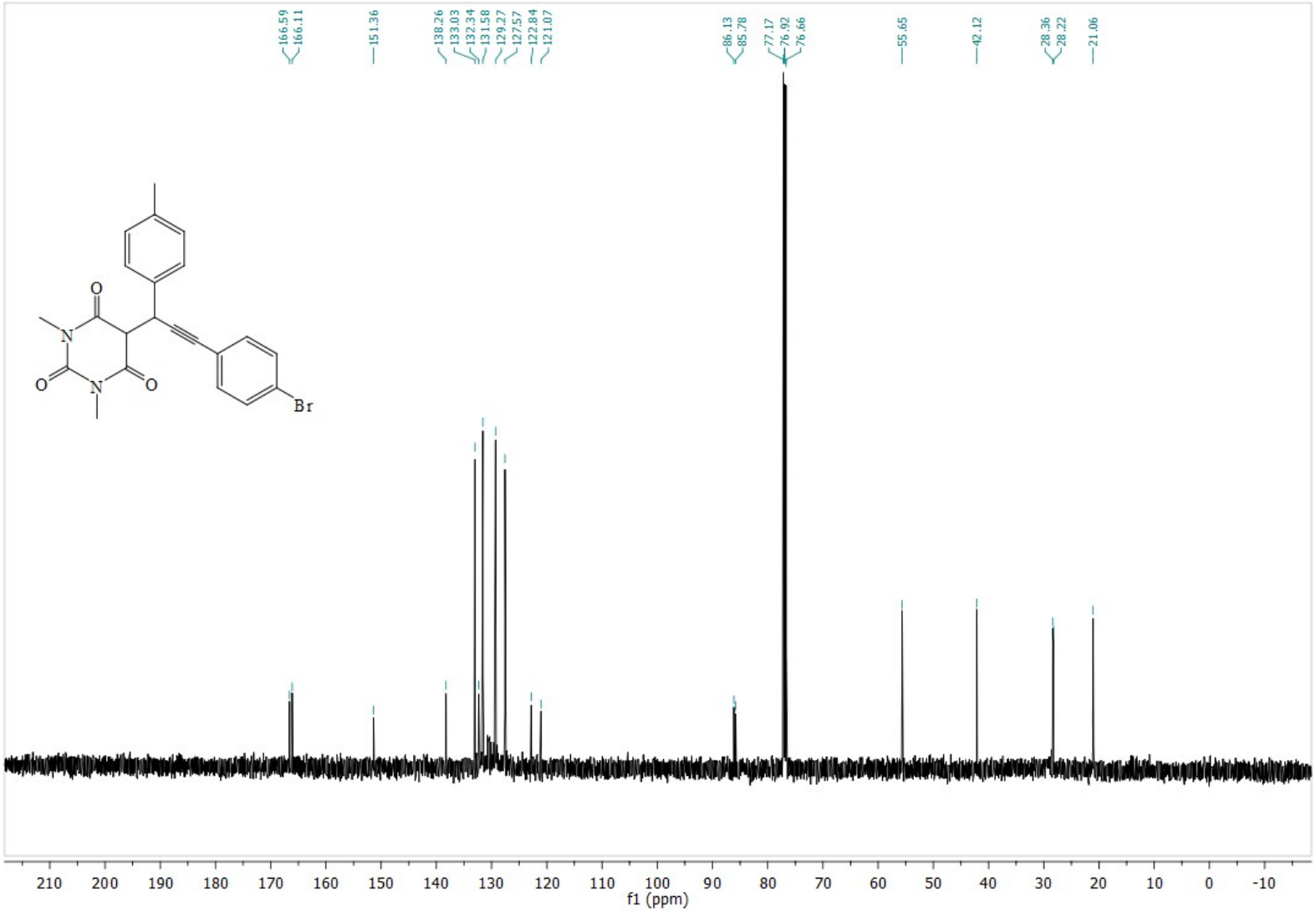
^{1}H NMR Spectrum of compound 4a'



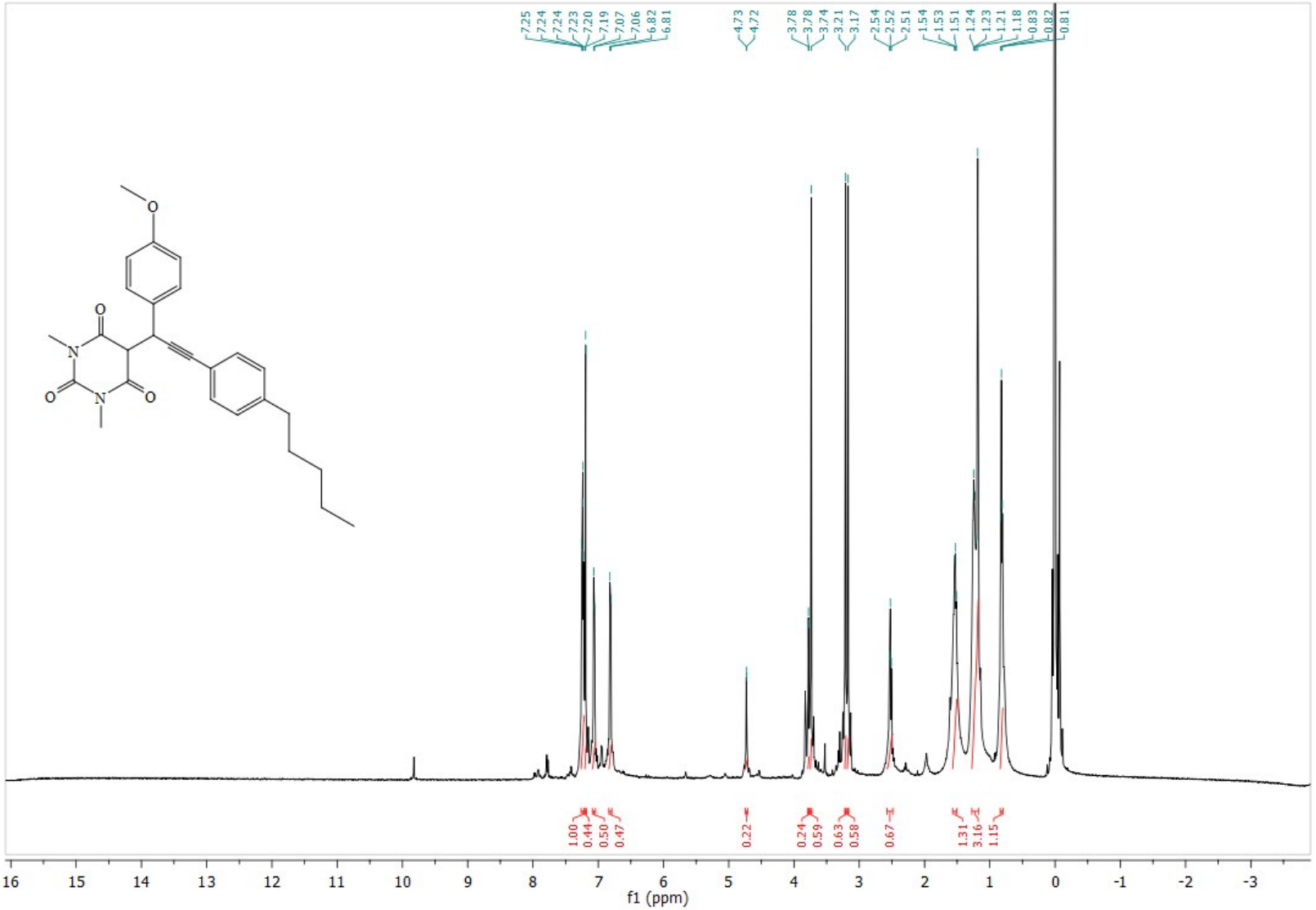
^{13}C NMR Spectrum of compound 4a'



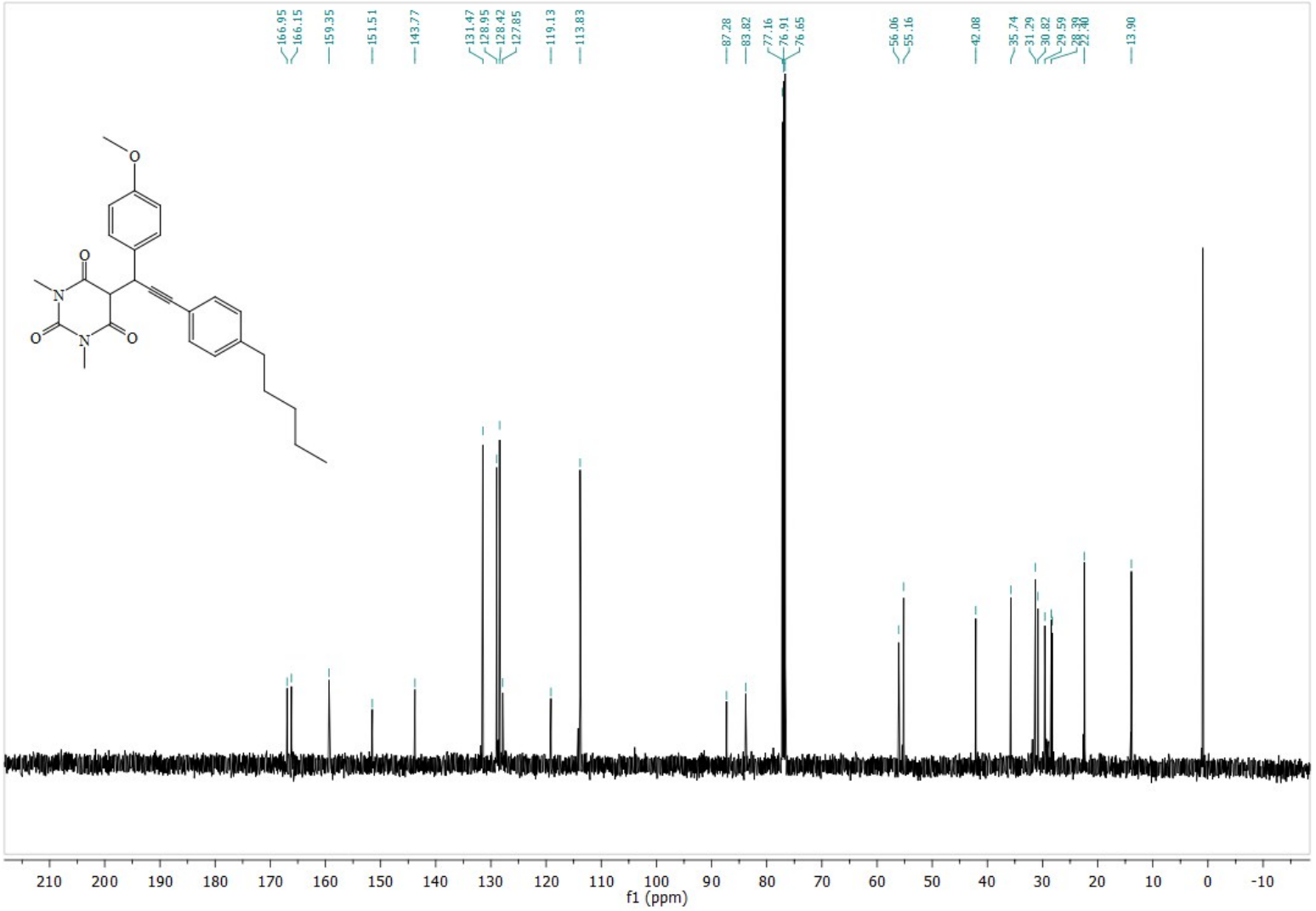
^{1}H NMR Spectrum of compound 4i'



^{13}C NMR Spectrum of compound 4i'



[1]H NMR Spectrum of compound 4x'



^{13}C NMR Spectrum of compound 4x'